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ARCHIVES OF SURGERY

VOLUME 20 APRIL, 1930 NUMBER 4

THE RECOGNITION OF ELEPHANTIASIS AND OF ELEPHANTOID CONDITIONS BY SOFT TISSUE ROENTGENOGRAMS

WITH A REPORT ON THE PROBLEM OF EXPERIMENTAL LYMPHEDEMA *

FREDERICK LEET REICHERT, M.D.

SAN FRANCISCO

Although elephantiasis has been described for centuries, the involvement of the lymphatics in this disease was not recognized until the extent of the lymph channels in the body had been revealed by the work of many anatomists, and until physicians in the tropics had found filarial organisms blocking the lymph vessels and lymph nodes.

THE LYMPHATIC SYSTEM

The universality of this system throughout the body was vaguely recognized in the eighteenth and nineteenth centuries. Until recently, knowledge of the lymphatic system was limited to anatomic studies of these thin walled valvular vessels in various parts of the body as demonstrated by the injection method. It was known also that there were two sets of lymphatics in the extremities, a superficial and a deep group which eventually drained into deeply situated lymph nodes. This is well illustrated in an old chart (fig. 1).

Of the many anatomists who have studied the lymphatics, one feels that if William Hunter had lived a little longer, he and his pupil Cruickshank would have contributed an earlier understanding of the importance of this system in its relation to the vascular system and in its economy in body function. By Hunter's death the work was left to Cruickshank, who, hampered by lack of funds, was able to prepare only a few sketches to illustrate his monograph on the lymphatic system. In the William Hunter Museum in Glasgow the many beautiful specimens of lymphatics filled with mercury stand today as ready to be carefully described and correlated as when they were prepared over a hundred years ago.

* Submitted for publication, Oct. 28, 1929.

* From the Halsted Laboratory of Experimental Surgery, Stanford University Medical School.

It remained for others in this country to repeat the injections made by these Glasgow anatomists. The first approach by modern investigators was made by studies of embryonic injections. Just as the origin of the arterial and venous systems had been revealed by embryonic studies, so the investigations of a number of workers, notably Sabin

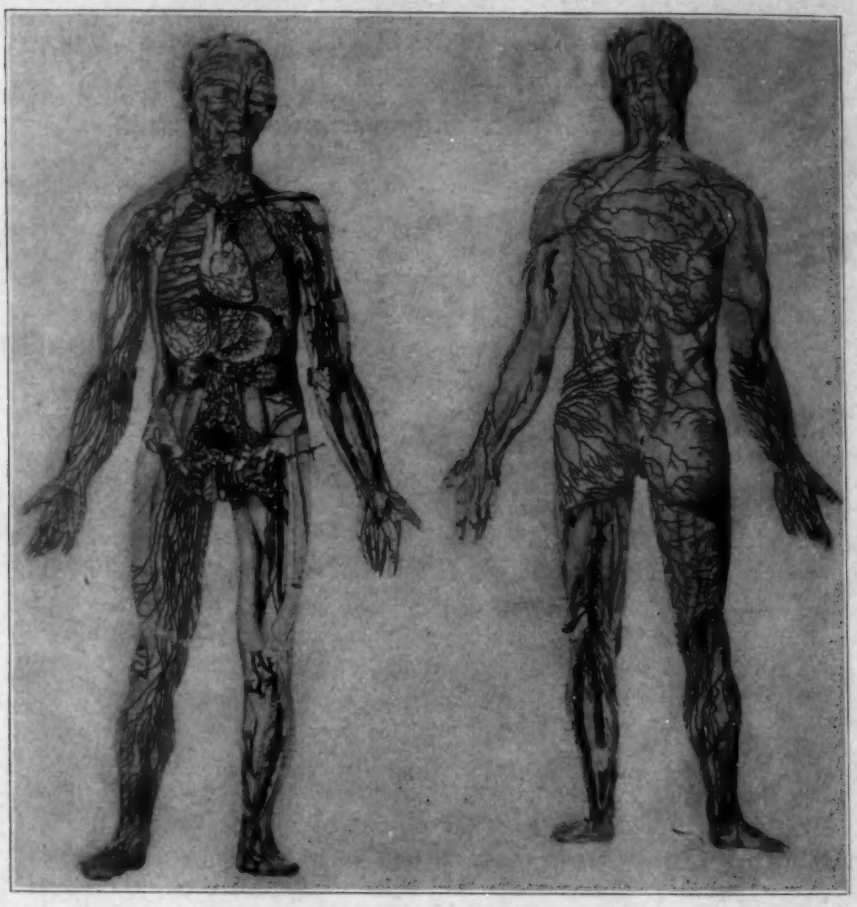

Fig. 1.—Old chart of the lymphatic system, showing the superficial and deep sets of lymphatics in the extremities which eventually drain into deeply situated lymph nodes.

and her pupils, present a fairly complete picture of the origin of the lymphatic system and its correlation with the lymphatics in the adult. It is known that as modified veins, lymphatics have a specific function in absorption although the complete physiology of this system is not as yet established.

The present teaching concerning lymphatics makes them a system as objective and definite as that of the arteries and veins. Just as there are definite blood capillaries, so there are definite lymphatic capillaries and tissue spaces. Sabin [1] suggested that if the name "plasma" is reserved for fluid within the blood vessels, "lymph" for the fluid within the lymphatics and "tissue fluid" for the fluids of the tissue spaces, conceptions would be greatly clarified. Just as blood capillaries grow through proliferation of their own walls and regenerate when divided, so do the lymphatic capillaries regenerate a little more slowly than the veins. Infection and scar tissue interfere with the growth of blood capillaries and likewise hinder the regeneration of lymphatic capillaries.

The importance of the lymphatic system in the maintenance of circulatory balance has been emphasized by Halsted,[2] and I have shown it experimentally.[3] A limb in its normal state requires a balance of the efferent vessels of the arterial system with the afferent vessels of the lymphaticovenous system. A disturbance on the afferent side may lead to edema as a result of venous or capillary derangement or it may be caused by lymph stasis. Frequently this edema is due to disturbances of the interdependent lymphatic and venous systems.

THE EDEMAS

True lymph edema, caused by division or blockage of lymph channels, usually involves both the dermal and the subcutaneous structures but not the deeper tissues. It produces a brawny, leathery condition of the integument, and the dermal distention often gives an "orange peel" appearance to the surface of the skin. There is no definite pitting on pressure of the skin. It occurs after bilateral glandular dissection of the neck, particularly on the facial side of the incision and is not evident until the second postoperative day. It usually subsides completely within a week or ten days but may persist for two weeks or longer if the regeneration of lymphatics across the wound has been delayed by poorly approximated tissues or by infection. Lymphedema is sometimes seen in carcinomatous breasts, and it may produce the enlargement found in Milroy's disease, although in two of the three cases of this disease which I have seen, infection had been superimposed on this condition. Clark and Clark [4] experimentally produced generalized lymphedema by removal of the lymph hearts in embryos.

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1. Sabin, F. R.: The Growth of the Lymphatic System, The Harvey Lectures, 1915-1916, Philadelphia, J. B. Lippincott Company, p. 124.

2. Halsted, W. S.: Replantation of Entire Limbs Without Suture of Vessels, Proc. Nat. Acad. Sc. **8**:185, 1922.

3. Reichert, F. L.: The Regeneration of the Lymphatics, Arch. Surg. **13**:871 (Dec.) 1926.

4. Clark, E. W., and Clark, E. R.: The Character of the Lymphatics in Experimental Edema, Anat. Rec. **21**:127 (May) 1921.

Vascular edema, pitting edema or "dropsy," presents a different picture. This edema exists throughout all the structures, especially in the subcutaneous tissue and muscle, and does not particularly involve the dermis. The skin is tense and smooth and pits readily on pressure. The edema is usually more marked in the lower extremities or limited to them, although it may be generalized. It diminishes readily when the part is elevated. It is generally the result of capillary damage and stasis in cardiovascular or renal disease and can be produced by division or blockage of all the veins to a part.

Neither lymphedema nor vascular edema, even of long duration, will lead to a proliferative change and deposition of fibrous connective tissue. When, however, infection or toxemia is superimposed on a derangement of the lymphaticovenous system, a condition of elephantiasis may develop.

ELEPHANTIASIS

Matas [5] gave a comprehensive definition and description of this condition:

> By elephantiasis we mean a progressive histo-pathologic state or condition which is characterized by a chronic inflammatory fibromatosis or hypertrophy of the hypodermal and dermal connective tissue which is preceded by and associated with lymphatic and venous stasis, and may be caused by any obstruction or mechanical interference with the return flow of the lymphatic and venous currents in the affected parts. In order to bring about the hypertrophy of the connective tissue, which is the distinct feature of the true elephantiasic state, the mechanical impediment to the lymphatic and venous drainage of the part is not sufficient, because a simple mechanical obstacle, while causing a regional or localized dropsy or lymphedema, will not bring about the characteristic fibromatosis and other histologic changes which are peculiar to elephantiasis. As Unna, Darier and many others have well shown, a simple mechanical edema is incapable of exciting a proliferation of the collagenous connective tissue. We know by clinical observation that edema may exist many years in the extremities and other parts without causing any fibromatosis or hyperplasia of the connective tissue of the parts. Something more than lymph stasis is required, and that something is infection with pathogenic organisms, and especially those of the streptococcal type which find a favorable soil for development in the stagnant lymph stream. The histopathological elements which are essential to complete the picture of elephantiasis are: (1) a mechanical obstruction or blockade of the veins and lymphatics of the region, usually an obliterative thrombo-phlebitis or lymphangitis or adenitis; (2) hyperplasia of the collagenous connective tissue of the hypoderm; (3) gradual disappearance of the elastic fibers of the skin; (4) the existence of a coagulable dropsy or hard lymphedema, and (5) a chronic reticular lymphangitis caused by secondary and repeated invasion of pathogenic microorganisms of the streptococcal type.

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5. Matas, R.: The Surgical Treatment of Elephantiasis and Elephantoid States Dependent upon Chronic Obstruction of the Lymphatic and Venous Channels, Am. J. Trop. Dis. & Prev. Med. **1**:60 (July) 1913.

We have now come to realize that whatever the cause of the lymphedema may be, the element of infection is the one essential and determining factor in the production of true elephantiasis. In fact, if we accept the views of many writers such as Le Dantec, Sabouraud and Unna, the progressive fibromatosis which we recognize as elephantiasis nostros, may occur independently of any stagnatory state of the lymphatic or venous circulation, and solely as a result of repeated attacks of a streptococcal infection, which has been regarded by many as identical with the erysipelas coccus of Fehleisen. Moreover, the streptococcal infection of elephantiasis presents all the characteristics of the classical cutaneous erysipelas, with the exception that in elephantiasis it is usually limited to one particular region in the lower extremity, the eruption rarely extending beyond the groin.

That it is in the highest degree probable that the true sporadic cases of elephantiasis develop from incompletely healed erysipelas—that is, those which leave behind disturbances in the circulation. The streptococci remain latent in the tissues and in this way excite the chronic proliferative tissue changes which we subsequently recognize as elephantiasis. At first the attacks of erysipelas occur at long intervals, perhaps twice or three times a year, then once a month, rarely oftener. Each time the limb grows larger until in the course of time a distinct elephantiasic state is established. Natural immunity does not appear to be easily acquired; and once the erysipelatous habit, so-called, is acquired, it usually becomes a permanent feature of the disease, though in some cases the attacks become milder and disappear altogether, but not until the elephantiasic state is fully established.

Halsted,[6] in considering the swelling of the arm after the radical operation for cancer of the breast, showed "that excision of the axillary and supraclavicular glands plus resection of the subclavian and axillary veins is rarely followed by noticeable swelling of the arm. On the other hand we do not deny that obstruction of these lymphatic and venous channels might conceivably alone, without infection, suffice occasionally to produce a moderate amount of oedema." His records tend to show that in all cases in which the swelling in the arm persisted, infection had been the main factor in its production and he termed this chronic indurated enlargement, elephantiasis chirurgica. As he pointed out, many of the patients gave an account "of recurrent attacks of redness and increased swelling accompanied by digestive and constitutional disturbances. These attacks not infrequently ushered in by chills and fever" occurred at infrequent intervals from months to years apart.

This reaction, which accompanies the appearance of the local erysipelatous rash, is what Sir Joseph Fayrer termed elephantiasic fever. As Matas stated:

The fever usually lasts from two to eight days and defervesces with the subsidence of the erysipelas which rarely extends beyond the root of the limb. During the attack, the skin of the affected region becomes red, painful, swollen and looks exactly like the erysipelas rash; the lymph nodes are enlarged and the red-

6. Halsted, W. S.: The Swelling of the Arm After Operations for Cancer of the Breast—Elephantiasis Chirurgica—Its Cause and Prevention, Bull. Johns Hopkins Hosp. **32**:309 (Oct.) 1921.

ness diffuses itself with great rapidity over the entire surface of the limb. After the subsidence of the attack, the skin remains swollen, giving the impression of a soft, doughy oedema. The soft consistency gives place to a more permanent hardness, the skin of the affected part never returning to normal. The underlying soft parts unite with the skin, which increases very much in thickness, forming a firm, immovable mass of tissue which continues to grow until it finally assumes a monstrous size which is characteristic of the disease.

Bertwistle and Gregg [7] agreed that elephantiasis develops only "in cases of solid oedema after attacks of fever and lymphangitis." Considering the pathology of the disease, they stated:

> It appears necessary, therefore, that not only must there be a transudate of lymph, but that it must be changed in some way, as happens when it becomes an exudate as the result of inflammation. It has been shown that the lymph exudate in cases of elephantiasis is charged with albumin, and, as protein is a stimulent to cell activity and growth the key to the hypertrophy and hyperplasia probably lies in Starling's description of the function of lymph: "The only way the tissues can receive their supply of protein is from the small amounts which are filtered through the blood vessels into the lymph. The increased exudation of concentrated lymph which occurs in inflammatory conditions as the result of injury is therefore of advantage, since it furnishes an abundant supply of protein food to be used up in the regeneration of the damaged cells." In elephantiasis the affected part receives an increased supply of protein as the result of recurring attacks of inflammation, and it is suggested that this protein, instead of merely helping in the process of repair, serves by its continuous or prevented action to stimulate the connective tissues to excessive growth.

Some writers think that the toxemia produced by the death of the filarial organisms, rather than the infection, is the factor in causing elephantiasis tropicum. Bertwistle and Gregg mentioned a case reported by Manson-Buhr in which elephantiasis followed the toxic absorption of chrysarobin in the treatment for psoriasis. I have the records of two cases in which excision of the axillary lymph nodes was done, and in which incipient elephantiasis was present due to repeated attacks of malaise, fever and vomiting associated with pain and swelling of the affected extremity following the eating of shellfish. The excision was done in one case for carcinoma of the breast, and in the other for epithelioma of the hand.

EXPERIMENTAL WORK ON ELEPHANTIASIS [8]

According to Unna,[9] it would seem that Bockhart, Sabourand, Le Dantec and others have tested the development of elephantiasis in man

7. Bertwistle, A. P., and Gregg, A. L.: Elephantiasis, Brit. J. Surg. **16**:267 (Oct.) 1928.

8. The earlier portions of this investigation were carried on in the Hunterian Laboratory of Experimental Surgery, Johns Hopkins Medical School, with the assistance of Dr. Mont Reid and Dr. C. Y. Bidgood in 1920.

9. Unna, P. G.: The Histopathology of Diseases of the Skin (Translated by N. Walker), New York, The Macmillan Company, 1896, p. 493.

by inoculation of pure erysipelas cultures, but so far as I know experimental elephantiasis has never been produced in animals.

Attempts to produce elephantiasis in experimental animals were initiated by Professor Halsted in conjunction with his study on elephantiasis chirurgica following radical mammary amputations. The posterior extremities of cats and dogs were chosen as the most satisfactory operative area, and we first tried to produce edema by complete excision of the iliac and inguinal lymph nodes without success. Nor did it occur following ligation of the iliac or the femoral vein with excision of the regional lymph glands. We then attempted blocking the lymphatics by injections of gelatin, agar, paraffin, celloidin, bismuth and india ink into the lymphatic channels and lymph nodes. Only a slight transient swelling followed these methods of injection.

Finally, Professor Halsted suggested a transverse division of the thigh as a means of severing all lymphatics. The first experiment was made by Dr. Mont Reid, and as he feared possible gangrene only a hemicircular division of the thigh was done. Again only a very slight edema appeared, and as neither gangrene nor infection developed, the rest of the limb was severed ten days later, leaving only the femur, femoral artery and vein intact. A definite swelling occurred distal to the incision and persisted for several days, and for the first time a marked lymphaticovenous edema had been secured.

With improved technic a complete severance of the thigh by circular incision was performed at one operation, leaving in continuity only the carefully denuded femoral artery and vein and the femur stripped of periosteum (fig. 2 in my previous work [8]). All bleeding points in the muscle were tied off with fine silk and the limb was replanted by careful approximation of the aponeurosis of each muscle with interrupted fine silk sutures. The subcutaneous tissue and skin were likewise approximated with interrupted silk sutures. As a result of the most rigid aseptic technic and gentle handling of the tissues, these replantations healed per primam and with a minimum of scar formation, in the great majority of the experiments.

Invariably edema appeared in the replanted limbs on the second postoperative day, reached a maximum on the fourth or beginning of the fifth day and had subsided completely by the seventh or eighth day (fig. 2). By the use of Hill's [10] opaque roentgenographic mass injected into the arterial system, new arterial anastomoses were demonstrated at the end of the second day and were numerous on the third postoperative day. When a warm gelatin mass of lead chromate was injected through the arteries and capillaries into the venous system of the limb, new

10. Hill, E. C.: Notes on Opaque X-ray Mass, Bull. Johns Hopkins Hosp. **35**:218 (July) 1924.

venous anastomoses across the replanted area were evident at the end of the fourth and the beginning of the fifth day, just when the swelling, as indicated by measurements, had reached a maximum or was beginning to subside. Further proof of venous regeneration was shown by the fact that for the first time since replantation, ligation of the only patent venous channel, the femoral vein, could be attempted without the development of gangrene. This procedure did not cause further edema; in fact, there was a delay of only one or two days in the subsidence of the swelling.

A previous report [8] offers these replantation experiments as a comparatively easy method for investigating the regeneration of both the superficial and the deep sets of lymphatics under what may be consid-

Fig. 2.—Photograph of a replanted limb when the lymphaticovenous edema was about maximum.

ered normal conditions. The earliest lymphatic regeneration was shown to be four days after operation, at which time the new venous channels were also being formed. These new lymphatics were demonstrated in the superficial group, and by the eighth day, when the edema had completely subsided, regeneration was physiologically adequate in both the deep and the superficial sets of lymphatics. At this time ligation of the femoral vein caused no recurrence of the edema, but swelling reappeared when the lymphatics were blocked with granules of india ink. Evidently, then, the lymphatic system by its regeneration was of importance in producing a subsidence of the edema, and with the veins formed a lymphaticovenous system, the function of which lay in disposing of the edema and in reestablishing the circulatory balance. The experimental results of a study of the circulatory balance in these replanted limbs will be presented in another paper.

Delay in the subsidence of the swelling was secured in some cases at the time of operation, when long silk ligatures were loosely placed about the femoral artery and vein to facilitate the location of these vessels at a later date. The edema persisted for two weeks or more in these limbs, although there was no infection. In the region of the vessels, the silk had caused an inflammatory reaction which, as shown by injections of india ink, had interfered with the regeneration of the deep set of lymphatics.

In other experiments, attempts were made to delay the regeneration of the superficial set of lymphatics by the formation of considerable scar tissue in the skin and subcutaneous layer. The irritants used to produce the cicatrix were the actual cautery, or chemicals, such as carbolic acid and alcohol, iodine and indelible ink. When no infection occurred, edema remained for ten days or more and injections of india ink showed that a number of superficial lymphatics were blocked at the line of incision.

When the regeneration of both the superficial and the deep sets of lymphatics was interfered with there was a delay of from two to three weeks in the subsidence of the edema. In all these experiments, and in those in which infection of the wound occurred, the edema disappeared completely.

By such experiments we felt that a lymph and venous edema had been produced. Examination of the replanted limb at the fourth or fifth postoperative day demonstrated the edema existing throughout all the tissues. In the late stages of a delayed edema, such as that produced by interference with the regeneration of the lymphatics, the edema was mainly confined to the skin and subcutaneous tissues, being more nearly a pure lymphedema.

Infection superimposed on such an edema seemed the next step in the production of an experimental elephantiasis. It was hoped that repeated streptococcal inoculations would lead to the enlargement and fibromatosis of elephantiasis, but during the past eight years we have failed in its production although we have tried many methods of inoculation and have sought the advice of a number of bacteriologists. Dogs seem to be exceedingly resistant to streptococcal infections, the inoculations producing abscesses rather than lymphangitis. Occasionally veterinarians have had cases of canine lymphangitis, but either cultures were not taken or we were not able to secure live organisms. Our inoculations were made with streptococci obtained from patients with scarlet fever and erysipelas, grown in twenty-four hour broth culture and then centrifugated to concentrate the bacteria. Injections were made both intradermally and subcutaneously in many replanted limbs at a time when the edema was subsiding or just after its disappearance. In only

one instance did an animal develop a lymphangitis, which spread over the white skin of the fox terrier like an erythematous rash and was followed by desquamation. Repeated inoculations brought no repetition of this canine scarlet fever.

Other methods, such as injections of the bacteria into the femoral artery and the distal veins of the replanted limbs and inoculations into excoriated skin areas, failed to initiate any evidence of lymphangitis.

The next step would seem to be the repetition of replantation experiments in an animal species more subject to lymphangitis.

THE ELEPHANTOID CONDITION

Elephantoid conditions are frequently seen and have been recognized by Matas [5] as follows:

> But the majority of cases that come under our observation are elephantoid states, swollen limbs, and genitals, following chronic lymph oedemas of the dependent parts in which venous and lymphatic obstruction plays the leading rôle in the pathogeny. The starting point of these obstructions may be traced to injuries involving the circumference of the limbs at their root, or tumors blocking the deep lymphatics; chronic circular ulcers of the leg, syphilitic, tuberculous and phagedenic in origin; chronic phlebitis associated with varices, post typhoid; puerperal; chronic eczema and kindred conditions. In the upper extremity the arm and the hand are often seen swollen and brawny, with chronic lymph oedema in women who have neglected cancer of the breast and whose axillary vessels have been compressed by cicatricial contraction or by secondary neoplastic metastasis. These elephantoid states constitute an extremely unsightly, painful and disabling deformity which in the lower extremities. especially, restrict the patient to a sedentary life.

Emphasis has again been placed by Homans,[11] Traut [12] and myself [13] on the common failure to recognize these frequent elephantoid conditions. Homans expressed the belief that a disturbance of the lymphatics underlies the process in thrombophlebitis of the deep veins of the legs (phlegmasia alba dolens). The milk leg is not cyanotic, as one would expect if only a great extent of vein were thrombosed. He attributed the white swelling to the inflammatory process associated with the thrombosis which promptly involves the accompanying principal lymphatic trunks which drain the limb, thus producing a lymph stasis of the entire extremity. Experimentally, he produced "milk leg" of ten days'

11. Homans, J.: Thrombophlebitis of the Lower Extremities, Ann. Surg. **87**: 641 (May) 1928.

12. Traut, H. H.: Ulcers Due to Varicose Veins and Lymphatic Blockage; A New Principle in Treatment, Arch. Surg. **18**:2281 (June) 1929.

13. Reichert, F. L.: Circulatory Disturbances of the Extremities with Special Reference to Thromboangiitis Obliterans and Elephantoid Conditions, California & West. Med. **31**:233 (Oct.) 1929.

duration in a dog by introducing 2 cc. of muscle juice into the lumen of an isolated segment of femoral vein. The resulting inflamed segment and perivenitis presumably blocked the adjacent lymphatic trunks, although this was not demonstrated by injection of these lymphatic vessels.

Working with Zollinger, Homans [14] extended his experiments and secured a transient lymph stasis due to demonstrable lymphatic blockage.

In 1926, I attempted to produce "milk leg" experimentally by inducing venous thrombosis. Only a slight transient swelling of the thigh developed after the injection of nonhemolytic streptococci or *Staphylococcus aureus* into isolated segments of the iliac vein. A moderate edema of the thigh, leg and foot of from four to seven days' duration followed intravenous injections of 20 per cent saline solution. In some instances venous thrombosis and perivenitis developed. The salt solution was kept within the vein for twenty minutes either by a tourniquet at the level of the groin or by the isolation of a portion of the external iliac vein between clamps. Cauterization of the vein with ensuing thrombosis and perivenitis was obtained by introducing a silver wire from a diathermy machine into the lumen of the saphenous and femoral veins. This resulted in an edema of the whole limb which lasted for eighteen days. Four days after cauterization a small hematoma appeared deep in the thigh which may have been a factor in the production of the perivenitis although there was no increase in the edema.

As Homans stated, the complication that occurs after phlegmasia alba dolens is usually "a porky oedema in the superficial tissues of the calf. . . . This oedema sooner or later becomes indurated, the skin over it pigmented, and if the patient must spend much time in standing, the indurated area finally breaks down wholly or in part and becomes an obstinate ulcer." His postphlebitic indurations are really localized elephantoid areas.

Traut emphasized the importance of lymphatic blockage in the production of ulcers due to varicose veins. Both he and Homans advocated the removal of this elephantoid tissue, including the underlying muscular aponeurosis.

I agree with Matas that the chronically enlarged indurated legs, often with resistant ulcers, the background of which is the story of phlegmasia alba dolens, of long-standing varicose veins or of chronic infective processes of a pyogenic, syphilitic, tuberculous or fungoid nature, are in truth evidence of an elephantoid condition, differing from elephantiasis only in their extent and ulceration. The same chronic, inflammatory fibromatosis exists in true elephantiasis, and one generally secures a history of infection or a story of repeated attacks of erysipelas.

14. Homans, J., and Zollinger, R.: Experimental Thrombophlebitis and Lymphatic Obstruction of the Lower Limb, Arch. Surg. **18**:992 (April) 1929.

SOFT TISSUE ROENTGENOGRAMS

When Professor Halsted was so interested in elephantiasis, a few roentgenograms were taken of the involved limbs, which showed a great thickening of the superficial tissues. Since then all of our cases of an elephantoid nature, as well as some cases of edema due to cardiovascular or renal disease, have been roentgenographed to outline the tissues, and the films have been carefully studied. I [13] think that roentgenograms taken to define the soft tissues rather than bone offer a means of clearly differentiating the edema of an elephantoid nature from other types of edema. Roentgenograms of simple lymphedema show an enlargement of the tissues from the skin to the muscular layer, whereas the films of ordinary dropsy or vascular edema show a diffuse density or thickening which involves all of the tissues of the extremity.

In contrast with simple lymphedema, elephantiasis and elephantoid states present an entirely different picture in soft tissue roentgenograms. Not only do they show a great thickening of the dermis and marked enlargement of the subcutaneous tissues down to muscle with a thickened muscular aponeurosis, but the unique feature in this condition is an extensive network of fibrous trabeculations in the hypodermal layer. This roentgenographic reticulation is produced by the marked fibromatosis of the subcutaneous layer. Only in case of elephantiasis or elephantoid conditions do the roentgenograms reveal these trabeculations. These characteristic trabeculations were also found in the roentgenograms of a youth seen on the pediatric service with a familial history of bilateral congenital "lymphedema." No history of attacks of elephantiasic fever or infection of the leg was obtained, and the patient was considered as having an uncomplicated case of Milroy's disease.

REPORT OF CASES

A few selected cases, with their soft tissue roentgenograms, will serve to illustrate simple edema, elephantiasis and elephantoid states.

CASE 1.—G. O., a man, aged 50, for years had suffered from glomerulonephritis and for the past five months had had a continuous pitting edema. Soft tissue roentgenograms revealed a diffuse homogeneous cloudiness throughout the swollen leg. The roentgen appearance (fig. 3) was typical of that seen in edemas due to cardiovascular or renal disease.

CASE 2.—In M. N., a woman, aged 71, a carcinoma of the uterus was removed seventeen years before examination, with no subsequent difficulty. Since menopause, at the age of 55, she had felt a small hard lump in the right breast which was diagnosed as a "hardened milk duct." The lump was traumatized four years before examination and had since gradually increased in size. Two years later, a mass appeared in the right axilla followed by pain in the breast. One year prior to examination, the cancer in the breast ulcerated and for the first time swelling of the hand and arm appeared. Figure 4 shows the ulcerative mammary carcinoma

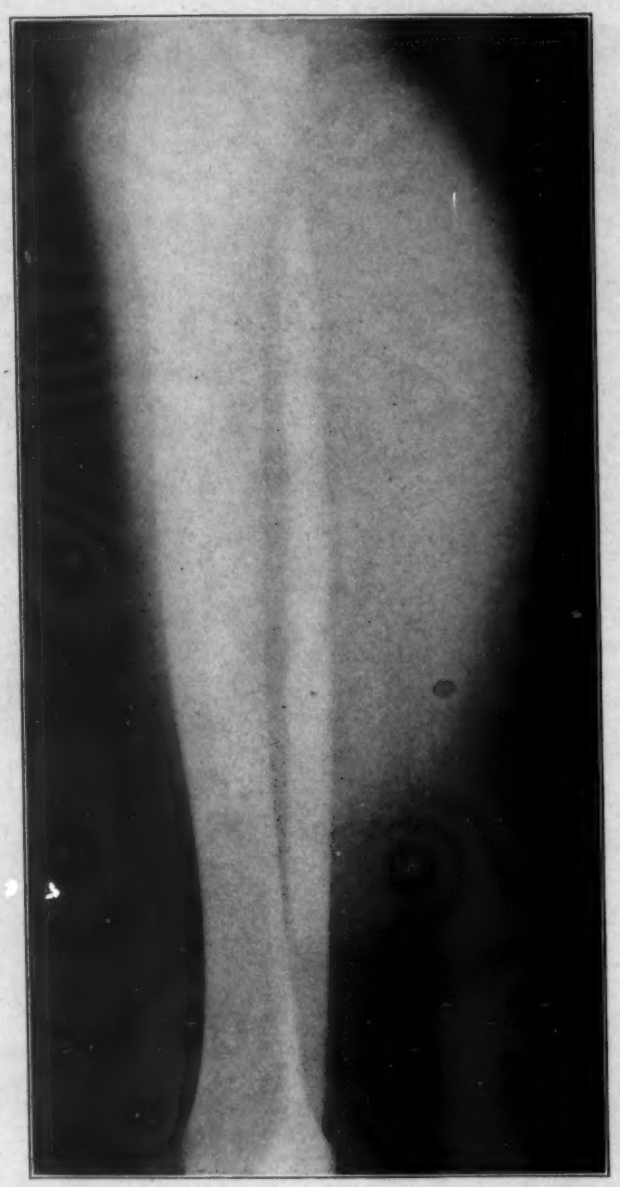

Fig. 3 (case 1).—Soft tissue roentgenogram to show diffuse homogeneous cloudiness throughout the swollen leg, typical of vascular edema.

with a large, hard, axillary metastasis firmly attached to the skin and deeper structures. The entire right upper extremity was enlarged and indurated. Although the right and left arms appeared to be of about the same size, the right was much heavier and felt boardlike, with a thick leathery skin and an indurated hypodermal layer. This enlargement of the extremity appeared only after the carcinoma had ulcerated and become infected. No history of an elephantiasic fever could be obtained.

A diagnosis of elephantiasis of the extremity was made and was confirmed by the soft tissue roentgenograms (figs. 5 and 6). In order to make a reproduction similar to the original roentgenogram and to prevent loss of detail, the photographic reprints have been retouched. Dr. R. R. Newell's report of the roentgenograms is as follows: Both arms were very large. There was a rather marked

Fig. 4 (case 2).—Right ulcerated mammary carcinoma, with axillary metastasis and elephantiasis of the right upper extremity.

contrast in the appearance of the two, however. The consistency of the left was rather smooth. The muscles could be seen overlying the bone, and in the very thick fatty layer branched vessels could be traced quite clearly. He believed that he could identify the cephalic and basilic veins. The consistency of the subcutaneous layer in the right arm was different, however, being markedly reticulated. The directions of the fibers were irregular, but on the whole were rather at right angles than parallel to the humerus. On account of these reticulae and the slightly greater density, the veins did not stand out as clearly as they did in the left arm. The forearms showed the same contrast in the appearance of the soft parts as did the upper arms, but in much more marked degree. Trabeculation of the subcutaneous tissue in the right arm was very coarse and heavy; on the whole it was irregular in orientation, but was inclined to be arranged vertical to the length of

the arm rather than parallel to the surface of the skin. No definite changes in the bone were made out, except for some sharpening of the left coronoid, attributed to chronic arthritis.

CASE 3.—H. M., a woman, aged 63, had suffered from varicose veins in the right leg for the past forty-eight years, and for several decades eczema had persisted on the medial surface of the leg. Three years before examination the eczematous area was severely scratched, and an ulcer formed. No swelling of the leg was noted at that time. In another hospital, the ulcer was treated by compresses followed by varicotomy. The convalescence was stormy, with fever and

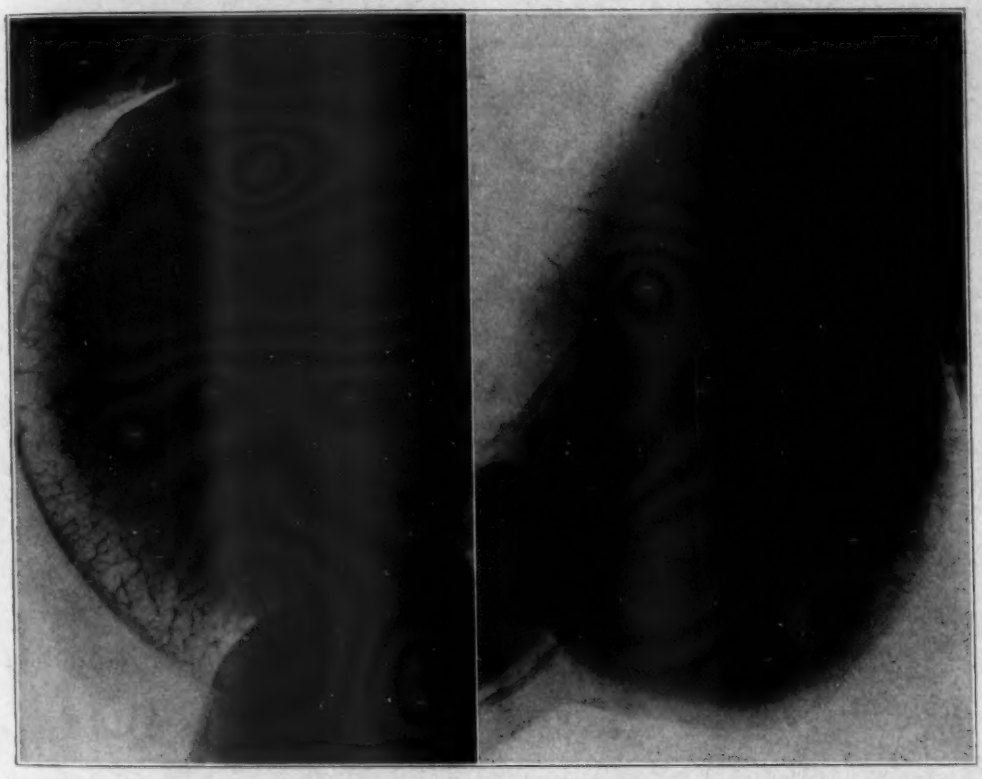

Fig. 5 (case 2).—Retouched print of soft tissue roentgenograms of the right and left arms. Although of about the same size, the right arm shows the typical trabeculations in the subcutaneous layer characteristic of elephantiasis.

bilateral pleurisy, and the limb became swollen and painful. She was unable to walk for three months and since then the leg and thigh had remained swollen, with persistence of the edema. One year prior to examination, because of pain and redness in this limb, an incision was made for pus, but the diagnosis was given as *Streptococcus cellulitis*. The eczema continued uncontrolled, with frequent small excoriations. The extremity had gradually enlarged, with the development of a brawny edema and a thick leathery skin, as shown in figure 7.

The diagnosis of elephantiasis of the right lower limb was confirmed by the soft tissue roentgenograms (fig. 8).

Case 4.—W. T., a woman, aged 47, following a laceration of the left leg thirty-two years before examination, suffered from considerable swelling and inflammation which remained for a few weeks. Four years later a more or less continuous edema first appeared, and since then she had suffered from several attacks of local inflammation in the leg attributed to scratches or trauma. At the age of 39, following pregnancy the enlarged superficial veins in that limb became thrombosed followed by greater swelling of the leg. Two years before examination, after an attack of "blood poisoning" in the leg, an ulcer appeared on the skin and the edema became more severe. Although the ulcer healed she had had seven or eight subsequent inflammatory attacks, the last one being diagnosed as erysipelas. All of these were initiated by malaise, chills and fever, nausea and vomiting and reddening of the skin of the leg with intense itching. After each attack the limb was heavier and more painful, and the skin was thick and hard to dent. The patient was seen at the end of the last attack, during which the reddish eruption and erythema had spread upward to the left groin and on the upper part of the right thigh. The entire left extremity was markedly swollen, red and hot. The skin and subcutaneous layer were indurated and twice as thick as on the right side.

Fig. 6 (case 2).—Retouched print of soft tissue roentgenograms of the right and left forearms. A very coarse and heavy subcutanoeus trabeculation is present in the elephantiasic forearm.

A diagnosis of elephantiasis with elephantoid fever was made. This was substantiated by the appearance of the soft tissue roentgenograms (fig. 9).

Case 5.—H. T., a man, aged 73, five years before examination noticed a small wartlike growth on the sole of the right foot which gradually increased in size.

Two years later, this cancerous growth was excised, and the area was grafted with the Thiersch graft. Six months later the wound broke down, with a recurrence of the tumor accompanied by chills, fever and swelling of the leg. Infection continued, and the foot and leg remained swollen. Recently, enlarged inguinal glands were felt. The lower leg showed brawny induration of the skin and underlying tissues, but this did not extend into the enlarged thigh (fig. 10).

The diagnosis was: infection of recurrent epithelioma of the foot, with an elephantoid condition of the foot and lower leg. Soft tissue roentgenograms (fig. 11) showed considerable trabeculation of the thickened hypodermal tissue, especially marked in the lower half of the right leg.

Fig. 7 (case 3).—Elephantiasis of the right lower limb in a patient with a history of varicose veins, eczema of the leg and attacks of lymphangitis.

Case 6.—D. S., a man, aged 57, had been troubled with bilateral varicose veins for a number of years. An eczematous condition of the skin led to ulcerations of both legs. On the right, the ulcer healed for a time, and when first seen there was an old, pigmented, indurated scar on the right leg while the ulcer on the left leg, which had resisted all manner of treatment for twelve years, measured 5 by 3.5 cm. The tissues about the ulcer were indurated and firm, in places boardlike to palpation, with an edema involving the knee and thigh. Large tortuous varicose veins were seen on both limbs. After two months of treatment in the outpatient clinic, the ulcer measured 3 by 2.5 cm. and then became larger. The patient was then hospitalized (fig. 12). At this time, soft tissue roentgenograms showed some

remarkable calcifications in the legs and considerable irregular trabeculation in the subcutaneous tissues, more marked on the left.

After the ulcer was treated with surgical solution of chlorinated soda, the varicose veins were thrombosed by injections of hypertonic saline solution and small deep skin grafts were applied to the ulcerated area. A month later, a photograph (fig. 13) showed the healed ulcer with a diminution in edema and absence of varicose veins. Four months later, the elephantoid condition was greatly improved, the tissues were considerably softer with no evidence of edema and the ulcer remained healed.

Fig. 8 (case 3).—Retouched print of soft tissue roentgenograms of both legs, with the heavily reticulated hypodermal layer on the right side indicative of elephantiasis.

TREATMENT

From the previous discussion of elephantiasis and elephantoid conditions and a study of the case reports, one is struck by the relative frequency of these conditions and by the fact that through neglect or carelessness they have been allowed to develop on the common and often readily remedied disturbances of the venous and lymphaticovenous systems.

The importance of preventive measures is clearly indicated. Varicose veins are the precursors of distressing edema, indolent ulcers, painful indurations and, finally, elephantoid states. Once infection appears, hyperplasia of the connective tissue elements is sure to follow and is difficult to eliminate without radical surgical measures. So, too, do the chronic bacterial, fungoid and malignant ulcerations lead to the same sequelae with either an elephantoid state or elephantiasis as the

Fig. 9 (case 4).—Retouched print of soft tissue roentgenograms of both legs of a patient with a history of varicose veins and ulcer and recurrent attacks of elephantiasic fever in the left lower extremity. There are marked hypodermal trabeculations in the affected limb. (From California & West Med. **31**:233 [Oct.] 1929.)

final result. As Homans [11] emphasized, more care must be exercised in the early treatment for phlegmasia alba dolens if one is to prevent the later development of elephantiasis.

The recently popularized method of obliterating varicose veins by means of sclerosing solutions affords an ambulatory treatment for this

Fig. 10 (case 5).—Patient with infected malignant ulceration on the sole of the foot with inguinal metastasis, enlargement of the whole right extremity and an elephantoid state in the foot and lower leg.

Fig. 11 (case 5).—Untouched print of soft tissue roentgenograms of both legs, showing the heavy trabeculations of an elephantoid condition in the lower half of the right leg.

Fig. 12 (case 6).—Patient with bilateral varicose veins and chronic ulcer on the left leg of twelve years' duration.

Fig. 13 (case 6).—Patient one month after thrombosis of the varicose veins and epithelization of the ulcer on the left leg, showing marked improvement in the edema and elephantoid condition.

condition, to which patients readily consent, and in this way the incapacitating sequelae can be prevented. Patients with ulceration need immediate care directed to the healing of the ulcer and obliteration of the veins, for the longer the ulcer persists the more the fibromatosis develops and the limb remains in a potential elephantoid state. At times the base of the indolent ulcer is so indurated and devitalized that skin grafting is unsatisfactory unless excision of the ulcerated and fibrosed area and the thickened underlying aponeurosis is resorted to, as advocated by Homans and Traut.

For the late complications of phlegmasia alba dolens, Homans reported some success in overcoming the persistent swelling by the excision of strips of deep fascia for some distance above and below the edema. When the tissues are indurated or ulcerated, he included the fascia of the muscle in the excision.

Of utmost importance is the prevention of infection in a limb edematous from derangement of the lymphaticovenous system. Eczematous regions must be carefully treated and other areas of focal infection must be eradicated in order to eliminate the recurrent attacks of fever and lymphangitis. Vaccine therapy and injections of antistreptococcal serum have been used to advantage and have frequently aborted further attacks of elephantiasic fever.

As to the methods of treatment for elephantiasis, the best results are obtained by surgical procedures. Matas [5] gave an historical résumé of the surgical treatment and expressed the belief that the Kondoleon procedure is the most encouraging. Bertwistle and Gregg [7] agreed that the Kondoleon operation offers a good prospect of prolonged temporary, if not permanent, cure. After ten years of experience with this operation, Sistrunk [15] expressed the belief that it is of much value in dealing with this disease; his admirable illustrations perhaps describe the operation better than words.

Kondoleon [16] devised the operation in order to reestablish connections between the deranged superficial lymphatic system and the uninvolved deeper set of lymphatics. By removing a large amount of aponeurosis covering the muscles, he hoped that connections would be established between the two lymphatic systems. At the same time a large amount of skin and subcutaneous tissue was removed to decrease the size of the limb, and then the edges of the skin were approximated. This procedure was accomplished in several stages on both sides of the thigh and leg.

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15. Sistrunk, W. E.: Contributions to Plastic Surgery: The Kondoleon Operation for Elephantiasis, Ann. Surg. **85**:185 (Feb.) 1927.

16. Kondoleon, E.: Die Lymphableitung, als Heilmittel bei chronischen Oedemen nach Quetschung, München. med. Wchnschr. **59**:525 (March 5) 1912.

No proof is available that connections are established between the two sets of lymphatics by this operation, and that it is this regeneration and refunctioning of the superficial lymphatic group that leads to the marked improvement following this operation. Examination of several of these cases five and six years after operation strongly suggests that this improvement is largely due to the mechanical removal of a great amount of the diseased tissue, namely, removal of the skin, subcutaneous tissue and muscular aponeurosis, the only structures pathologically involved in this condition.

SUMMARY

The lymphatics, as a system of vessels and capillaries, are considered as objective and definite as the arteries and veins, and their growth and regeneration normally as well as in the presence of scar tissue is similar to that of the vascular system. Their importance in the maintenance of circulatory balance is emphasized.

True lymphedema is differentiated from vascular or pitting edema by its restriction to and induration of the skin and subcutaneous tissues. No edema even of long duration will lead to a proliferative change and deposition of fibrous connective tissue.

Elephantiasis is caused, not by lymph and venous stasis alone, but by its association with inflammation due to infection or toxemia. Chronic inflammatory fibromatosis of the dermal and hypodermal connective tissue is characteristic of this condition. The element of inflammation is the one essential factor in the production of elephantiasis. Elephantiasis tropicum, elephantiasis nostras streptogens and the elephantiasis chirurgica of Halsted all have the same pathologic background and differ only in the primary cause of the lymphatic and venous stasis.

The experimental work showed the importance of the lymphaticovenous system in maintaining circulatory balance. The production of lymphedema and lymphaticovenous stasis occurred in replanted limbs as well as by venous and perivenous blockade. Only one step, the induction of lymphangitis, apparently remains in obtaining experimental elephantiasis.

Elephantoid conditions are frequently seen, and emphasis is again placed on the importance of their recognition. The elephantoid state is a frequent sequel to varicose veins and phlegmasia alba dolens and to chronic bacterial, fungoid and malignant ulcerations.

Soft tissue roentgenograms of an extremity present a characteristic picture in elephantiasis and elephantoid conditions and serve as an adjunct in diagnosis and prognosis. The roentgenographic trabeculation in the hypodermal layer is produced by the fibromatosis in this tissue.

A few selected cases with their soft tissue roentgenograms serve to illustrate simple edema, elephantiasis and elephantoid states.

The importance of prophylactic measures is clearly indicated in the treatment for these conditions. In addition to preventive methods, such as the obliteration of varicose veins and epithelization of ulcers, the treatment for elephantiasis and elephantoid states by the Kondoleon procedure and its modifications is discussed.

GELATINOUS CARCINOMA OF THE BREAST *

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Gelatinous carcinoma [1] of the breast is a comparatively rare state. In a combined group of 2,944 carcinomas of the breast cited by Gaabe,[2] 49, or 1.66 per cent, were of the gelatinous type. Gelatinous carcinoma occurs in patients of about the same age as do the usual forms of carcinoma of the breast. Tumors undergoing gelatinous degeneration sometimes reach an enormous size and the mass of the tumor may consist largely of gelatinous material. On the other hand, the amount of gelatinous material may be so small that it may be readily overlooked. Similar degeneration is known to occur in tumors arising in other situations where mucin-forming cells abound, notably the large intestine, stomach and biliary tract.

Gelatinous carcinoma of the breast exhibits characteristic gross and microscopic appearances. The gross features may be striking. Large or small areas of the tumor may be somewhat translucent in appearance and may either consist of a light gray jelly-like substance or be light reddish brown. The gelatinous material may appear delimited by a more or less irregular outline. In the advanced stages, small and large tumors may fail to show any solid unaffected structure, the entire mass consisting of gelatinous material. On account of the innocent appearance of the lesion under these particular circumstances, an entirely false conception of the true state of affairs may be obtained from macroscopic examination alone.

Microscopically, gelatinous carcinoma of the breast has the usual appearance of carcinoma, in addition to which islands of degenerating and necrotic epithelial cells can be seen amid diffuse areas of gelatinous material. This material is typical in arrangement and appearance and requires no special stain in order for its presence to be detected. If a stain is desired, either mucicarmine or neutral red is appropriate.

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* Submitted for publication, Dec. 10, 1929.

1. The terms "colloid carcinoma" and "mucoid carcinoma" are also applied to this condition.

2. Gaabe, G.: Der Gallertkrebs der Brustdruse, Beitr. z. klin. Chir. **60**:760, 1908.

The prevailing opinion regarding gelatinous carcinoma of the breast is that it is the least malignant form of mammary carcinoma. According to this opinion, the disease is slower in its course, metastases occur later and the prognosis is more favorable than in the usual type. With few exceptions, the conception that this form of the disease may be highly malignant is not encountered in the literature. Several authors, however, have drawn attention to the highly malignant nature of some of these tumors (Despres,[3] Schmidt,[4] Gaabe[2]). Others, notably Lange,[5] while regarding these tumors as less malignant, admitted that the ultimate prognosis is not more favorable than in other types of carcinoma of the breast.

The first pathologic description of gelatinous carcinoma of the breast was attributed by Gaabe to Otto in 1816. The origin of gelatinous material in carcinoma of the breast is still the most interesting and disputed phase of the disease. The subject has been a matter of controversy since the condition was first recognized. Doutrelepont and Rindfleisch[6] attributed the formation of the gelatinous substance to an exudation of the blood plasma through the blood vessels with subsequent diffusion of the exudate into the tumor, a formation analogous to the process of edema. The chief point of dispute among pathologists is the question whether the connective tissue stroma or the epithelial cells of the tumor give rise to the gelatinous substance. The belief that the gelatinous substance originates in the connective tissue stroma has been held by Virchow, Meyer,[7] Kaufmann[8] and others. Lange was the first to study this problem by the use of a special stain (toluidinblau) and concluded that the origin of gelatinous material varied in tumors of different organs. In gelatinous carcinoma of the gastro-intestinal tract, he described a diffuse degeneration of the protoplasm of the tumor cells. In gelatinous carcinoma of the breast, the gelatinous degeneration occurred in the connective tissue, the tumor cells taking no direct part in the process. Lange's observations concerning the connective tissue origin of the gelatinous material were supported by Kaufmann who, on the basis of a study of five cases, reached a similar conclusion. From a study of four cases Ewing[9] concluded that the gelatinous degeneration

3. Despres: Traitê du diagnostic des maladies chirurgicales, Paris, 1886, p. 272.

4. Schmidt, G. B.: Diese Beiträge, vol. 4, 1888.

5. Lange, F.: Der Gallertkrebs der Brustdruse, vol. 16, 1896.

6. Doutrelepont and Rindfleisch: Arch. f. klin. Chir. **12**:551, 1870.

7. Meyer: Beiträge zur Histologie der schleimbildenden Adenome und Carcinome der Brustdruse, Diss., Rostock, 1880.

8. Kaufmann, E.: Lehrbuch der speciellen pathologischen Anatomie, ed. 3, 1904, p. 968.

9. Ewing: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1928.

had involved and partly originated in the fat tissue in the stroma. Borst [10] believed in a double origin from connective tissue and epithelial cells..

The notion that the gelatinous substance is the exclusive product of the epithelial cells is held by numerous authorities. Ribbert [11] noticed that in the early stages mucoid secretion begins in the lumen of the acini, whence it breaks through and infiltrates the surrounding connective tissue. Zimmermann [12] stated that the gelatinous substance was an epithelial cell product and pointed out the possible fallacies in the interpretation of reactions to special stains as performed by Lange. Finally Gaabe concluded that in most gelatinous carcinomas of the breast, the gelatinous substance begins as a degeneration and subsequent destruction of epithelial cells, without any active participation of the connective tissue. A gelatinous carcinoma of the breast with laminated calcified masses scattered through the tumor was depicted by Delafield and Prudden.[13]

The comparatively slow growth of gelatinous carcinoma of the breast was first pointed out by Lebert,[14] who described two cases in which the disease had lasted ten and twelve years, respectively. This observation was soon confirmed by Simmonds,[15] who reached similar conclusions after a study of twenty cases. The most extensive study of this subject was made by Lange [5] in 1896, when he reported seventy-five cases and by Gaabe in 1908, whose report comprised a study of sixty-nine cases of this form of carcinoma of the breast. Lange concluded that gelatinous carcinoma of the breast is more benign, grows more slowly and metastasizes more rarely than the usual forms of carcinoma of the breast. He pointed out the special tendency to late recurrence but concluded that the ultimate prognosis after operation is scarcely more favorable than in the usual forms of carcinoma of the breast. Gaabe's conclusions are essentially similar to those of Lange. His study of sixty-nine cases showed that gelatinous carcinoma of the breast differs from the usual type of carcinoma of the breast in the following ways: (1) the rate of growth is slower; (2) the invasion of skin, muscles and axillary glands and the development of ulceration occur two and one-half times as late; (3) recurrences appear later, and (4) the results

10. Borst: Geschwulstlehre, Wiesbaden, 1902.

11. Ribbert: Geschwulstlehre, Bonn, 1904.

12. Zimmermann: Ueber seltenere Formen der Brustdruseengeschwulste, Diss., Strassburg, 1902.

13. Delafield and Prudden (revised by F. C. Wood): A Textbook of Pathology, ed. 14, New York, William Wood & Company, 1928.

14. Lebert: Virchows Arch. f. path. Anat., 1852, vol. 4.

15. Simmonds: Deutsche Ztschr. f. Chir., vol. 20, p. 74.

of operation are at least twice as favorable, the operative cures being 51.43 per cent in gelatinous carcinoma against 25 per cent in the usual forms of breast carcinoma.

The fact that this form of the disease may be highly malignant is greatly obscured in the literature. Two references to this possibility, however, could be discovered. Despres [3] and Schmidt [4] pointed out that these tumors may be highly malignant and Gaabe stated that a gelatinous carcinoma may lose its gelatinous characteristics: its cells take on a high grade of anaplasia and the tumor may revert to a carcinoma of the usual type.

REPORT OF EIGHT CASES

CASE 1.—*Clinical History.*—A woman, aged 43 years, married, with two children, while in South Africa in July, 1928, noticed a painful lump in the right axilla which was rapidly increasing in size. At that time there were no clinical signs in the breast. The axillary mass was excised and on microscopic examination was found to contain carcinoma in a state of gelatinous degeneration. The patient was sent to London, where she was seen in consultation by one of us (G. L. C.) and by Mr. S. Cade (October, 1928). The breasts were very fat; there were no clinical signs of a tumor in the right breast, and no enlarged glands could be discovered in the right axilla and supraclavicular regions. There was no history of a discharge of blood from the nipple. A complete operation was performed on the right side. As a tumor could not be detected in the breast either before or after removal, whole microscopic sections of the gland were cut. Three months after the operation the patient returned with an extensive local recurrence in the skin and subcutaneous tissue. Mr. S. Cade treated the recurrence by means of external irradiation. The irradiation was followed by rapid and complete disappearance of the tumors. The regression was that of a highly radiosensitive tumor. The whole of the chest and mediastinum was subsequently treated with high voltage roentgen rays as a prophylactic measure by Dr. Finzi.

Pathologic Examination.—Figure 1 illustrates the whole microscopic section in which the lesion was discovered. At *B* a carcinomatous patch which had undergone gelatinous degeneration was discovered. Diffuse carcinomatosis in ducts and acini existed throughout the whole of this area of the gland. At *C* there was a dilated duct in which the tumor had undergone gelatinous degeneration. Figure 2 shows this duct magnified. The epithelial neoplasia within the affected ducts and acini and outside them exhibited the characteristic morphologic appearance of anaplasia. The growth was diffuse, the cells were small and highly atypical and mitoses were abundant.

We wish at this point to call special attention to the presence of two distinct types of malignant epithelial cells in this tumor. One type belongs to the common spheroidal cells; the other type presents morphologic features which differ from the usual appearance of anaplastic epithelial cells. The cells are somewhat larger, the nuclei stain darkly, vary in size and shape, are relatively small and may occupy the center of the cell, or they may be eccentric. The cytoplasm is acidophilic and homogeneous, and has well defined margins. The staining characteristics of the cytoplasm, the shape of the cells and the eccentric position of the nucleus give to some of the cells an appearance like that of a "plasma cell." They differ from plasma cells by being much larger. They possess the same degree of malignancy as the usual type of anaplastic cell, growing diffusely, dividing rapidly and infiltrating widely in small groups and singly.

No further involvement of axillary lymphatic glands was discovered by microscopic examination, although the lymphatic glands that were removed at the first operation contained extensive carcinoma which had undergone gelatinous degeneration.

Comment.—The inability to discover any tumor in the breast in case 1 on clinical examination may be accounted for in two ways: (1) by the adiposity of the breast, the layer of subcutaneous fat having

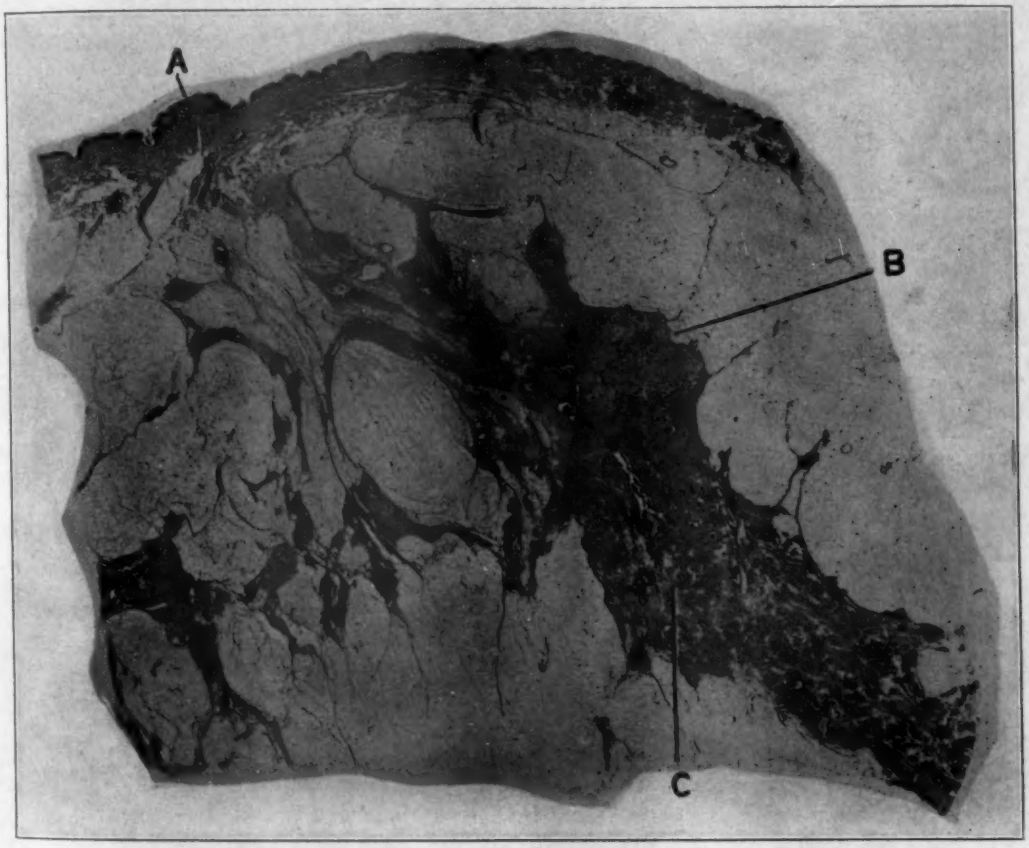

Fig. 1 (case 1).—Whole microscopic section of breast: *A*, nipple; *B*, site of gelatinous tumor; *C*, situation of duct, a high power magnification of which is shown in figure 2. The examination of these photgoraphs can be greatly assisted by using a hand lens. By this means the more minute details can be observed.

measured 3 cm. in thickness, and (2) by the fact that the carcinomatous parts adapted themselves to the contour of the breast, and therefore their presence was obscured on palpation. In fact, it was necessary to cut numerous serial sections of this gland before the tumor could be discovered. The size of the lesion is to a great extent accounted

for by the fact that an extensive and diffuse malignant epithelial neoplasia existed within the ducts and acini. In the duct shown here (fig. 2) the hyperplasia had undergone gelatinous degeneration. We regard the presence of gelatinous degeneration of the epithelial neoplasia within the duct as evidence in favor of our conviction that the epithelium can be carcinomatous even though it is still confined within normal boundaries. This belief is supported by the fact that the cells within the ducts that had not undergone gelatinous degeneration were in a highly anaplastic state. The first sign of disease was an enlargement

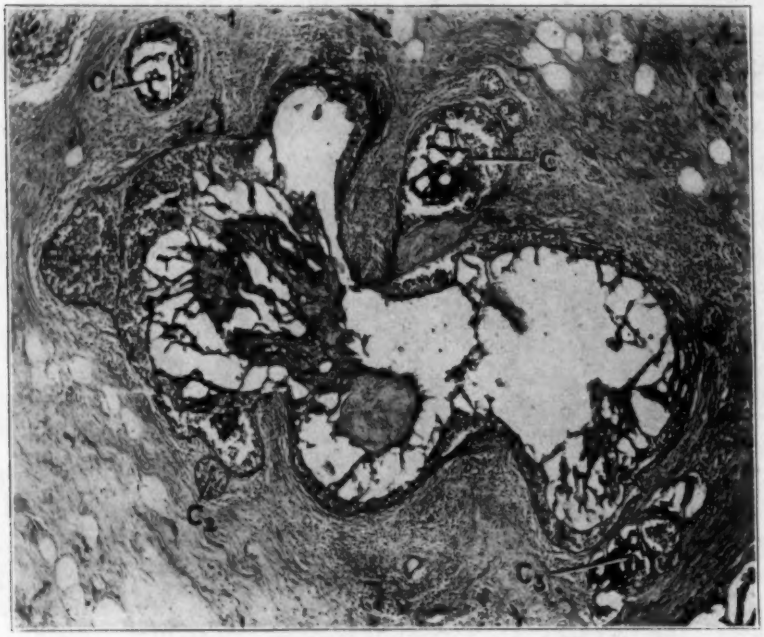

Fig. 2 (case 1).—Magnification of duct shown in figure 1 *C*. Gelatinous degeneration has occurred in the epithelial neoplasia with which it is filled. The same change is occurring in the acini *C* into which it branches. The elastica, unstained in this section, has undergone a slight degree of hyperplasia.

of an axillary lymphatic gland and there were no clinical signs of a tumor in the breast. Finally, it is necessary to draw attention to the marked radiosensitivity of this highly anaplastic tumor. In this example the intimate relationship that existed between the anaplastic histologic structure, the high degree of malignancy indicated by its early metastasis to a lymphatic gland and its marked radiosensitivity were completely demonstrated.

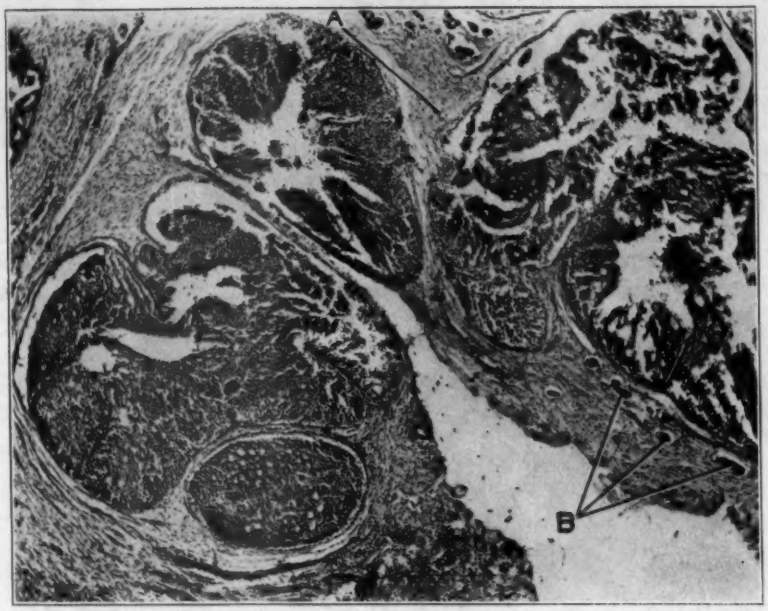

Fig. 3 (case 2).—*A*, ducts and dilated acini, some of which have become confluent. *B*, the epithelial elements in these structures consist of small round cells, crowded together with no definite arrangement, which are highly anaplastic in type.

Fig. 4 (case 2).—At *A* is a dilated acinus in which gelatinous degeneration has occurred in the epithelial cells, which fill and distend the structure, giving rise to a laciform appearance. At *B* the neoplastic epithelial contents of a duct are in an advanced stage of gelatinous degeneration.

CASE 2.—*Clinical History.*—A married woman, aged 44, with one child, noticed a tumor in the right breast eighteen months before operation. During this period she had been treated in India for "chronic mastitis." The breast was painful and there had been no discharge of blood from the nipple. Examination of the right breast revealed a large tumor 5 by 3 by 3 cm. occupying the outer middle segment. The mass was firm and nodular, and puckered the skin. The nipple was movable and not retracted. The axilla was filled with large, firm and discrete lymphatic glands. The supraclavicular glands were not palpable. The opposite breast and axilla were normal. Radical operation was performed. The patient died with visceral metastases nineteen months after the operation.

Pathologic Examination.—At least two ducts in immediate juxtaposition were full of epithelial neoplasia extending from immediately beneath the nipple into

Fig. 5 (case 2).—*A*, longitudinal section of a duct showing gelatinous degeneration of the epithelial cells within it: *B* and *C*, epithelial cells within acini undergoing gelatinous degeneration. The elastica of the duct has not been stained in this specimen but other sections show that it has undergone slight hyperplasia.

all their acini. One of these ducts, its branches and its acini could be traced with only slight interruptions throughout the whole course of its distribution. The other duct was not so completely demonstrated and only its beginning beneath the nipple could be seen. The chief mass of this tumor was due to epithelial neoplasia that was confined within the normal boundaries of the ducts and acini and epithelial invasion could be detected in only two places. The morphologic appearances of the epithelial neoplasia varied in different parts. In the terminal ducts and acini the cells were elongated and tapered. In some ducts papillomas had

formed with delicate stalks of connective tissue. Some terminal ducts and acini were distended by epithelial cells that were highly anaplastic in type (fig. 3 *A*). Within other ducts and acini the epithelial cells were arranged in a laciform manner (fig. 4 *A*). This peculiar formation was due to the gelatinous degeneration of epithelial cells, which caused the spaces among the remaining and unaffected parts. Gelatinous degeneration could be seen occurring in a more advanced state in many other isolated parts (figs. 4 *B* and 6 *A*). Most of the tumor had not undergone gelatinous degeneration. Gelatinous degeneration had occurred in the neoplastic epithelium contained in the duct shown in figure 5 *A*, and in the beginnings of two ducts beneath the nipple. The elastica had not undegrone hyperplasia and was normal in amount and distribution. The glands in the axilla were extensively affected by carcinoma and had not undergone gelatinous degeneration. Carcinoma had extended beyond the upper border of the first rib and the operation was unsuccessful in reaching the limits of the disease.

Fig. 6 (case 2).—*A*, gelatinous degeneration occurring in epithelial cells after they have invaded outside tissues; *B*, connective tissue which does not show any gelatinous degeneration.

Comment.—Except that the disease was more advanced in this tumor, it resembles that in case 1. The distribution of epithelial neoplasia confined within the ducts and acini was extensive in both specimens. It is remarkable that in so large a tumor there were so few sites of epithelial invasion of the stroma, especially when the lymphatic glandular involvement was so extensive. The explanation lies in the highly anaplastic state of the epithelial neoplasia in some parts of the tumor. The normal appearance and distribution of the elastica enabled us to trace the ducts and the acini and so to confirm our statement that the epithelial neoplasia contained within normal but distended boundaries

formed the main mass of the tumor. Microscopic examination of this tumor showed that the neoplastic epithelium was the first to undergo gelatinous degeneration and that this degeneration could begin in epithelial neoplasia when confined within normal boundaries. The laciform appearance of the neoplastic epithelium in parts of this tumor was due to the gelatinous degeneration of epithelial cells. A laciform appearance occurring in other carcinomas may be due to the union of anastamosing columns of epithelial cells or to a different type of degeneration occurring among them. The history of the patient demonstrates

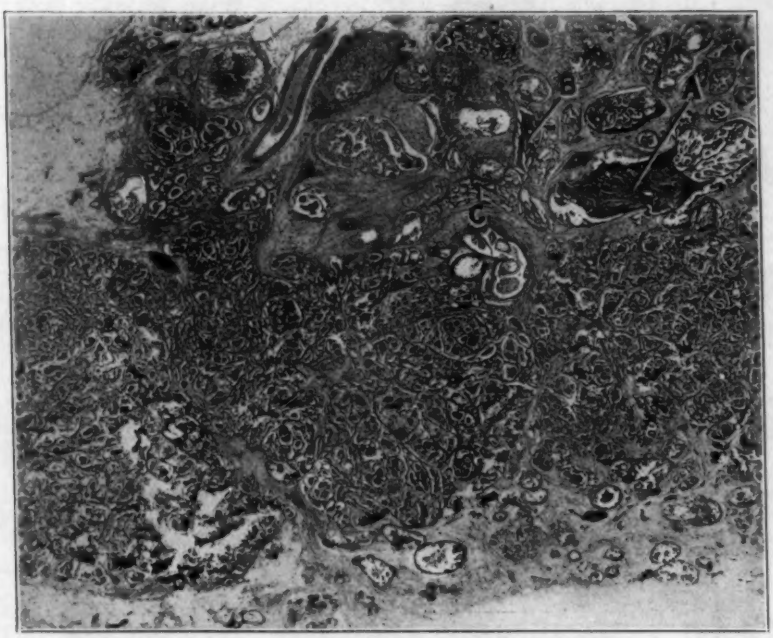

Fig. 7 (case 3).—Portion of a whole microscopic section. The ducts and acini are seen distended with neoplastic epithelium which in the duct *A* and its branches *B* and *C* have undergone gelatinous degeneration. The elastica, unstained in this section, has undergone a slight degree of hyperplasia.

the prevalent danger of trusting to a diagnosis of so-called chronic mastitis.

Case 3.—*Clinical History.*—A woman, aged 38, married, with two children, was sent home from India with a tumor about 2.5 cm. in diameter situated in the lower and outer segment of the right breast. This tumor had been noticed for about three months and was causing a localized stabbing pain. It was gradually increasing in size. There was no discharge from the nipple. On examination the skin puckered, the nipple was normal and the tumor was hard, nodular and freely movable. There was an enlarged, discrete, hard and tender lymphatic gland

beneath the outer border of the pectoralis major. There was no other adenopathy in the axilla or supraclavicular regions. The opposite breast was normal.

Pathologic Examination.—Microscopically, the lesion was more extensive than the clinical signs indicated. Figure 7 shows part of a whole microscopic section of the breast that was cut in a vertical plane parallel with the anterior surface of the body. Its general shape was triangular, with the apex toward the nipple. Although the main mass of the tumor was due to the presence of the epithelial neoplasia that was contained within the normal boundaries of the ducts and acini, there was also considerable epithelial invasion of the outside tissues. The epithelial neoplasia was not anaplastic in any part of the tumor. With this exception, it resembled the two tumors just described. Gelatinous degeneration was advanced in some parts of the tumor where cellular invasion had occurred. In other parts,

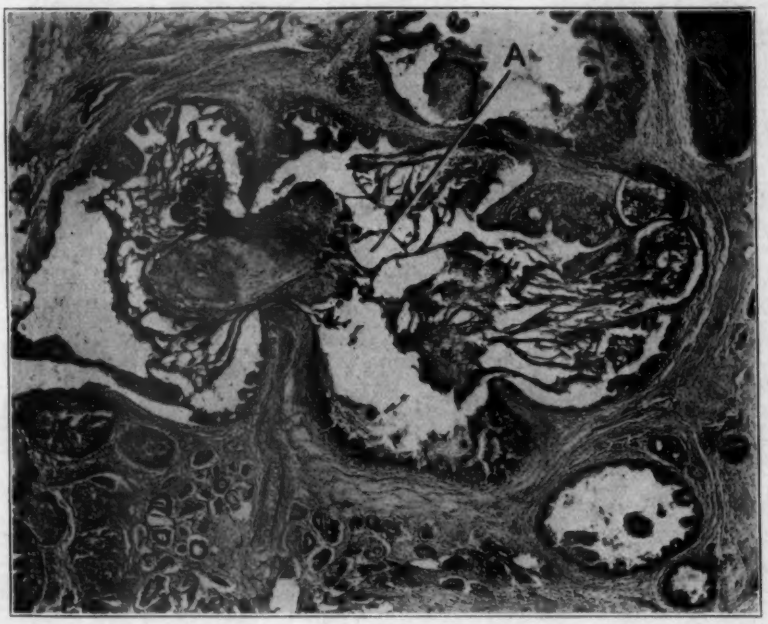

Fig. 8 (case 3).—Another duct in which the neoplastic epithelial content has undergone gelatinous degeneration.

the gelatinous degeneration was in an advanced state while still confined within the normal boundaries of the ducts and acini (figs. 7 *A* and 8). The elastica had not undergone hyperplasia and was normal in amount and distribution. The lymphatic gland in the right axilla was the only one affected and the carcinoma it contained had not undergone gelatinous degeneration.

Comment.—This specimen is another example of the wide distribution of malignant epithelial neoplasia that can be confined within normal boundaries. It also demonstrates gelatinous degeneration of epithelial neoplasia while it is thus confined, and shows that the gelatinous degeneration in its early states begins in the epithelium. It is an example of

gelatinous degeneration occurring in a carcinoma, the epithelium of which is not anaplastic. In this respect, it differs from the former two cases. This case also demonstrates that the primary lesion in the breast may be much more extensive than the clinical signs suggest. The patient is well and apparently free from disease five years after operation. In this respect it is interesting to point out that the tumor was not highly anaplastic, which probably accounts for the patient's present condition, even though one axillary lymphatic gland had been involved in the disease.

CASE 4.—*Clinical History.*—A married woman, aged 43, noticed a lump in the right breast six months before operation. On examination there was a hard, round

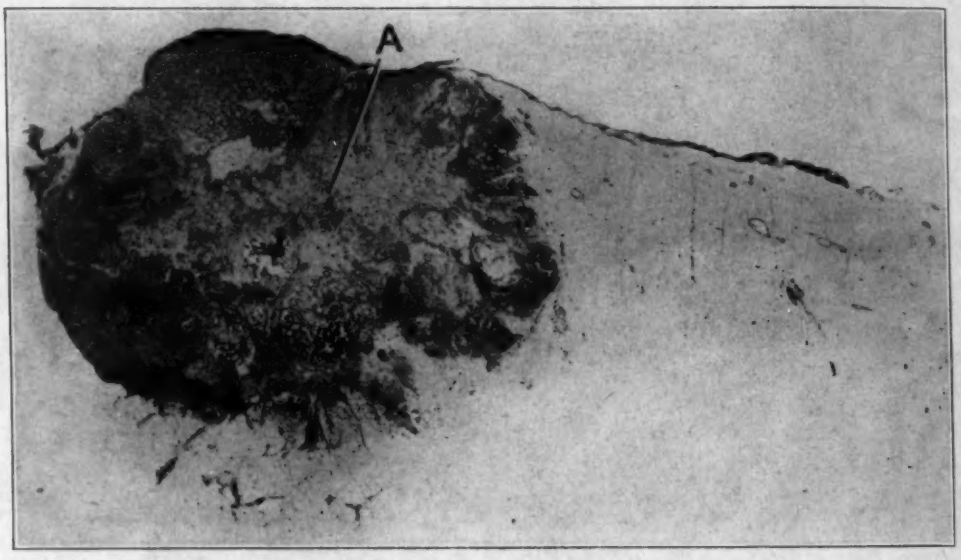

Fig. 9 (case 4).—Part of a peripheral portion of a breast which contains carcinoma. The central parts have undergone necrosis. At the margins the surrounding fat is being invaded by carcinoma. Gelatinous foci are shown in figure 10.

lump about 3 cm. in diameter, situated at the periphery of the outer segment of the breast. The skin was adherent to it. The nipple was not retracted and there was no discharge of blood from the nipple. The right axillary lymphatic glands were hard and confluent. There were no enlarged supraclavicular glands. The opposite breast was normal.

Pathologic Examination.—The tumor measured 2.5 cm. in diameter, was situated at the periphery of the breast and was composed almost entirely of epithelial cells that had invaded the stroma and the surrounding fat of the gland (fig. 9). The epithelium was highly anaplastic. Gelatinous degeneration had occurred in a small patch of the tumor that was detected only by microscopic examination

(fig. 10). Gelatinous degeneration had begun among small groups of cells adjacent to this patch (fig. 10, *A, B* and *C*). The lymphatic glands were extensively invaded.

Comment.—This specimen is another example of a highly anaplastic and malignant tumor that contains gelatinous degeneration. The carcinoma was advanced and had spread so diffusely that it had obliterated all signs of its primary site of origin. Where the gelatinous

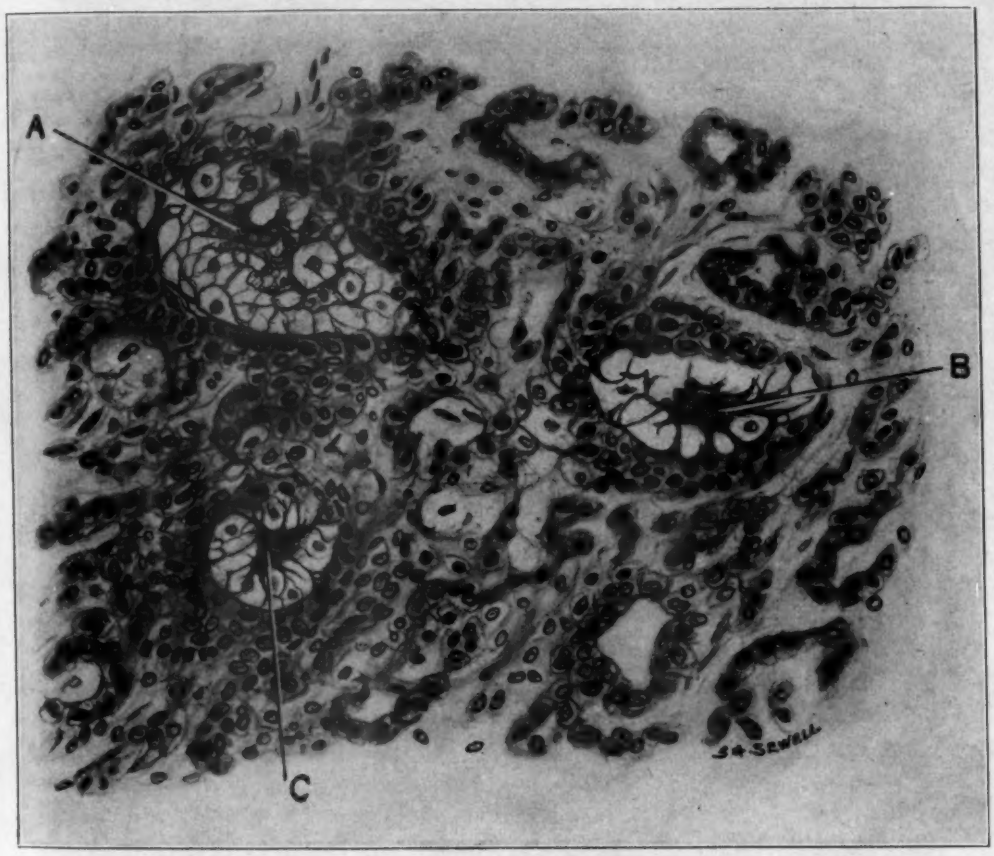

Fig. 10 (case 4).—Drawing, under high power, of three foci of gelatinous degeneration *(A, B, C)* occurring in the center of collections of epithelial cells that have invaded outside tissues. The drawing is made from the tumor shown in figure 9.

degeneration could be seen in the early stages, it was occurring in the epithelial cells. The patient died two and one-half years after operation of pulmonary metastasis.

CASE 5.—A married woman, aged 50, with no children, two years before admission noticed a lump to the right of the left nipple from which there was a discharge of blood which soon disappeared and never recurred.

Clinical Examination.—On the right of the nipple and in immediate juxtaposition to it there was a flat, round, firm swelling with well defined margins which pushed the nipple to one side. The skin was adherent to the tumor. The remainder of the breast was normal on palpation. The complete operation was performed on the assumption that the swelling beside the nipple was a duct carcinoma and was the cause of the discharge of blood from the nipple. During the operation the lymphatic glands in the axilla were discovered to be enlarged, hard and discrete. The thick layer of fat obscured their presence and prevented them from being felt on palpation.

Pathologic Examination.—Whole sections were cut of this breast, and the following conditions were revealed: The tumor beside the nipple was composed entirely of infiltrating carcinoma among which there was no sign of a duct. As

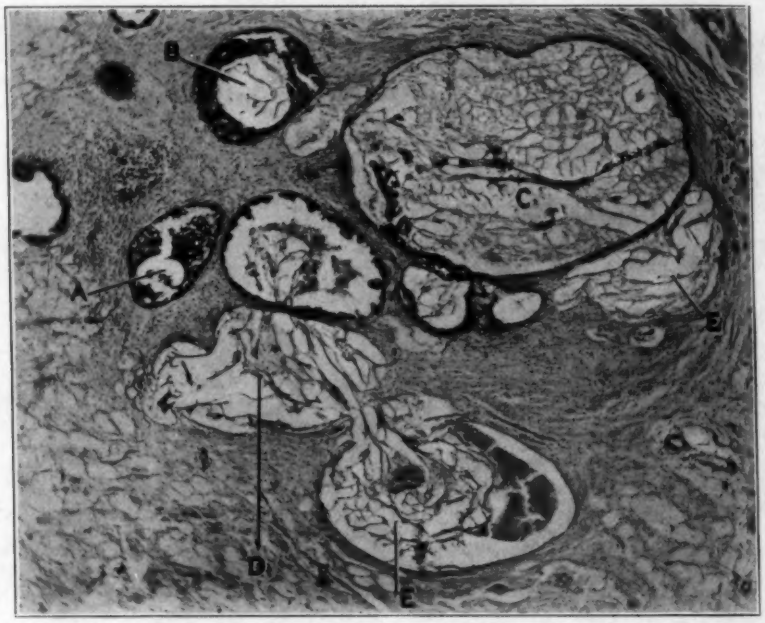

Fig. 11 (case 5).—A lobule in which various stages of gelatinous degeneration are seen in different acini: *A*, acinus in which gelatinous degeneration is in an early state; *B*, acinus in which the degeneration has occurred in the center, leaving layers of unaffected epithelial cells around its margin; *C*, acinus filled with and distended by gelatinous degeneration of epithelial cells, a few of which are still to be seen within the structure; *D* and *E*, acini which have become confluent and are filled by gelatinous degeneration only.

this discovery did not account for the discharge of blood from the nipple, more sections were cut in search of its cause. At the periphery of the outer middle segment of the gland, carcinoma was discovered affecting a large area of terminal ducts and acini. Many terminal ducts and acini contained epithelial neoplasia within normal boundaries. In a few small scattered parts of the stroma and surrounding fat, epithelial cell invasion had occurred. In the termnial ducts the epithelial neoplasia was chiefly papillomatous in type; in the acini it was sessile

only. In these parts the epithelial neoplasia looked malignant and in scattered areas had undergone gelatinous degeneration. Figure 11 shows four stages of mucoid degeneration which could be traced from its beginning to its final state. The earliest visible changes that could be detected may be seen in figure 12, which shows a terminal duct distended by epithelial neoplasia. The epithelium in this acinus contained many cells which were swollen and clearer than normal. The edges were well defined. The nuclei were smaller and appeared shrunken. A further stage of mucoid degeneration may be seen in figure 13 in an adjacent terminal duct which was distended by the same type of neoplastic epithelium. In the center of the acinus the final stages of gelatinous degeneration had been reached and several degenerated cells may be seen in the middle of the gelatinous material (fig. 13*B*). The surrounding cells were in the same state as the affected cells.

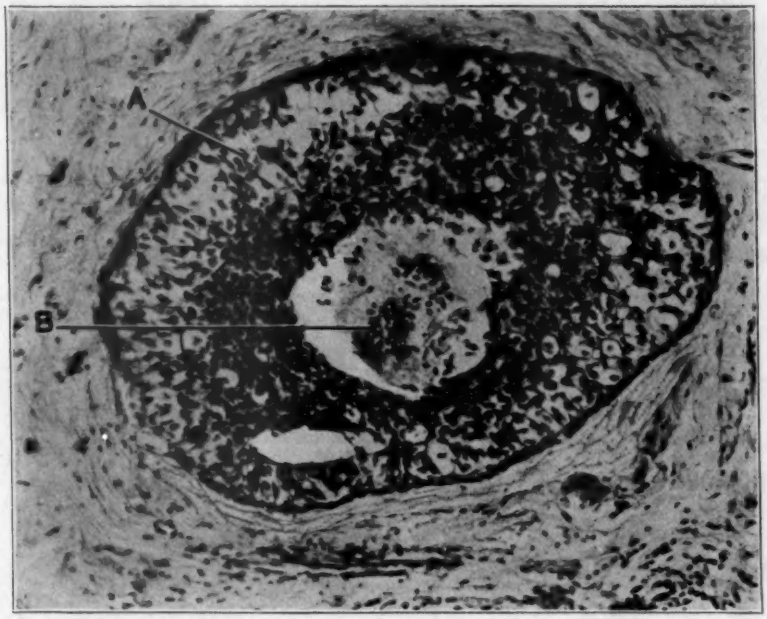

Fig. 12 (case 5).—High power magnification of a terminal duct distended by epithelial neoplasia. *A*, the marginal layers of epithelium show the earliest stage of gelatinous degeneration. The cells are swollen and the nuclei appear small and shrunken. At *B* in the center of the duct gelatinous degeneration is marked. The elastica around this duct has undergone hyperplasia.

Figure 11 shows a group of acini in all the stages of gelatinous degeneration, including its final phase. At *A* the process is in an early stage. At *B* it is more advanced and small islands of epithelial cells can be seen in the midst of gelatinous material, around the margins of which are epithelial cells which have not undergone complete degeneration. At *C* there is another acinus filled with and distended by gelatinous degeneration in which islands consisting of a few degenerated epithelial cells can be seen. At *D* and *E* gelatinous degeneration has extended to such a degree that no evidence of epithelial cells can be detected and the delicate gelatinous meshwork is all that can be seen.

Comment.—In this illuminating and interesting specimen the origin, course and final stages of gelatinous degeneration could be traced. The process began and ended in epithelial degeneration. The morphologic appearance exhibited an unbroken chain of events. The areas in which gelatinous degeneration appeared to have infiltrated the connective tissue stroma of the breast were really the remains of degenerated epithelium which had completely disappeared, leaving a gelatinous meshwork within the distended acinus. Gelatinous degeneration is not an infiltrating process and does not begin in the connective tissue; it is

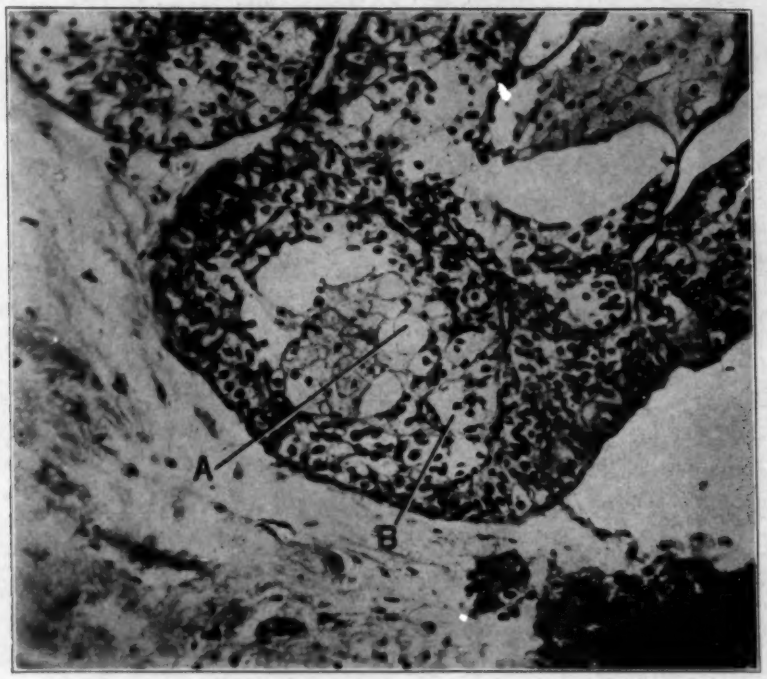

Fig. 13 (case 5).—High power magnification of terminal duct in which gelatinous degeneration has progressed farther than in the terminal duct in figure 12.

only an epithelial degeneration. Gelatinous degeneration can also occur in epithelial cells that have invaded normal structures. This degeneration occurring in carcinoma may give rise, as in case 6, to the appearance of a gelatinous degeneration beginning in or infiltrating connective tissue.

CASE 6.—*Clinical History.*—A woman, aged 42, married, with one child, had noticed pain in the right breast for twelve months. There was no discharge of blood from the nipple. On examination, a large tumor 3 cm. in diameter was found in the outer middle segment of the right breast. The nipple was movable

and not retracted. The tumor was adherent to the skin. The axillary lymphatic glands were hard, round and confluent near the breast. They were discrete and enlarged in the upper part of the axilla. The breast moved freely on the deeper structures. The whole breast was removed, and the patient died five years after the operation.

Pathologic Examination.—Whole microscopic sections showed that the tumor was large and triangular (fig. 14). The large size of the tumor was caused by the extensive epithelial invasion that had occurred in the stroma of the breast and

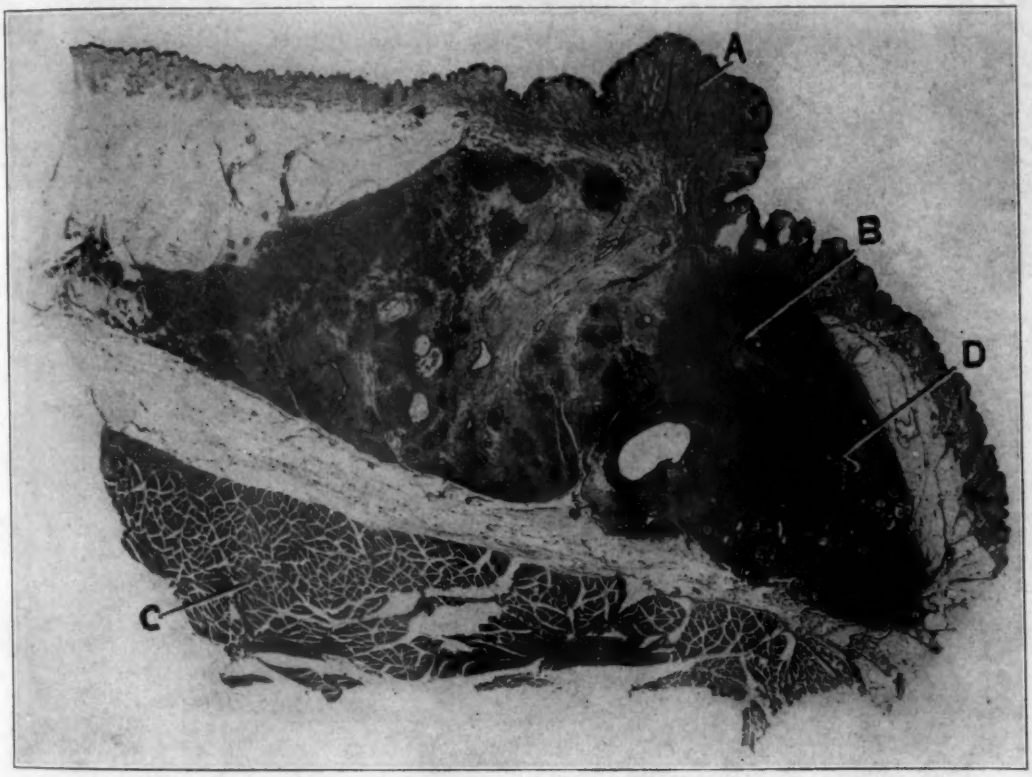

Fig. 14 (case 6).—Whole microscopic section of breast: *A*, nipple; *B*, tumor; *C*, pectoralis major; *D*, a large duct, a high power magnification of which is shown in figure 15. The neoplastic epithelium of this duct and its acini is the only seat of gelatinous degeneration that could be detected in this breast.

the fat immediately surrounding it. In other parts, malignant epithelial neoplasia could be seen distending the ducts and acini. In one of these ducts (fig. 15 *A*), it had undergone extensive gelatinous degeneration and islands of degenerated epithelial cells could be seen suspended in the typical gelatinous material. Figure 15 *B* shows that the acini which communicated with this duct had also undergone epithelial neoplasia and subsequent gelatinous degeneration. There was no other evidence of gelatinous degeneration in this tumor. The epithelial ele-

ments of the tumor were highly anaplastic. The elastica had undergone a certain amount of hyperplasia throughout the whole breast.

Comment.—This tumor has two points of interest: 1. The gelatinous degeneration was limited in extent; its presence was totally unsuspected and would probably have been missed had not whole microscopic sections of the breast been cut. 2. The epithelial elements of the tumor were highly anaplastic. The accidental discovery of the gelatinous degeneration in this tumor also suggests the probability that gelatinous degeneration may be more common than is generally supposed. The clinical history and microscopic appearances afford further evidence

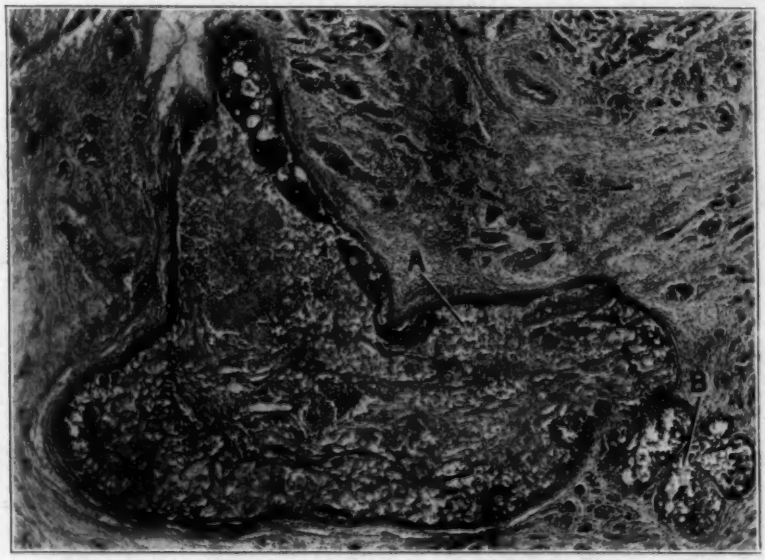

Fig. 15 (case 6).—High power magnification of duct (*A*) and its acini (*B*) taken from figure 14 *D*, showing large duct containing neoplastic epithelium, some of which has undergone gelatinous degeneration. Outside these structures carcinoma is rampant.

that carcinomas in which gelatinous degeneration has occurred can be highly malignant.

Case 7.—*Clinical History.*—A married woman, aged 45, with two children, noticed a lump in the left breast eight months before operation, during which time it gradually increased in size. On clinical examination, a large, hard, round tumor occupied the right side of the breast near the nipple. The skin was adherent to it. The nipple was movable and not retracted. The axillary lymphatic glands were not enlarged.

Pathologic Examination.—The tumor was large and round, measuring 3 cm. in diameter. To one side of and below its center was a large isolated area of gelatinous degeneration in which islands of degenerated epithelium could be seen (fig. 16). Disconnected strands of connective tissue could be seen amid the

gelatinous degeneration; they showed no sign of gelatinous change. The epithelium was not highly anaplastic. At the margin of the tumor ducts could be seen containing papillomas covered by three or more layers of epithelium. Sessile epithelial growth also existed in these ducts. The arrangement of the tissues composing this tumor was in many parts papillomatous, and its site of origin was undoubtedly one of the large ducts. There was extensive epithelial invasion of the stroma, but the surrounding fat had not been invaded. The axillary lymphatic glands were not invaded by the disease.

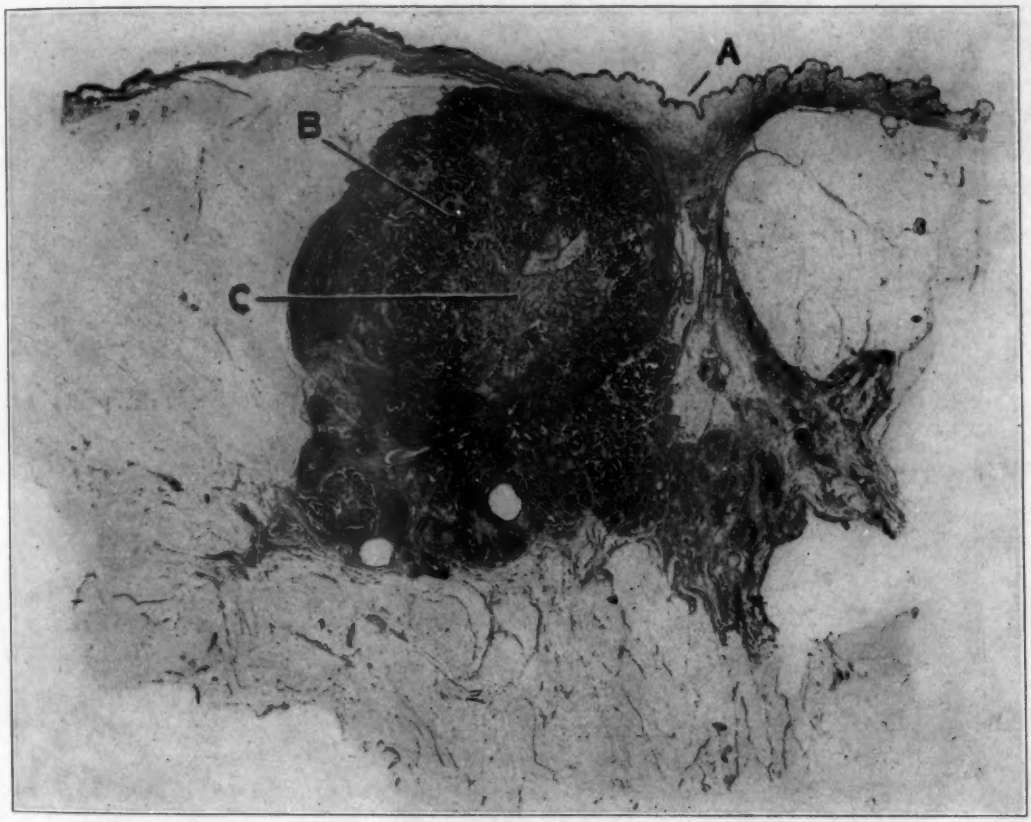

Fig. 16 (case 7).—Whole microscopic section of breast: *A*, nipple; *B*, tumor; *C*, site of gelatinous degeneration. The tumor is a large duct carcinoma in the center of which (*C*) gelatinous degeneration has occurred.

Comment.—This tumor belongs to the class in which gelatinous degeneration has occurred in a carcinoma that is not highly anaplastic. The carcinoma was not so rampant as to destroy all traces of its sites of origin in the larger ducts in spite of its large size. Its relatively

low state of malignancy was also indicated by the absence of lymphatic glandular involvement, although the tumor was a large one.

CASE 8.—*Clinical History.*—A woman, aged 57, married, with two children, complained of an aching pain localized to the middle outer segment of the left breast, which she had noticed for five months. She had also felt a lump in the breast and had noticed a brownish intermittent discharge from the nipple for the same period. On examination she appeared thin, and the breasts were small. On palpation, a localized, comparatively extensive area of fine nodularity was discovered in the painful part of the breast. It was not adherent to the skin or to the underlying tissues. The nipple was normal, and there were no enlarged glands

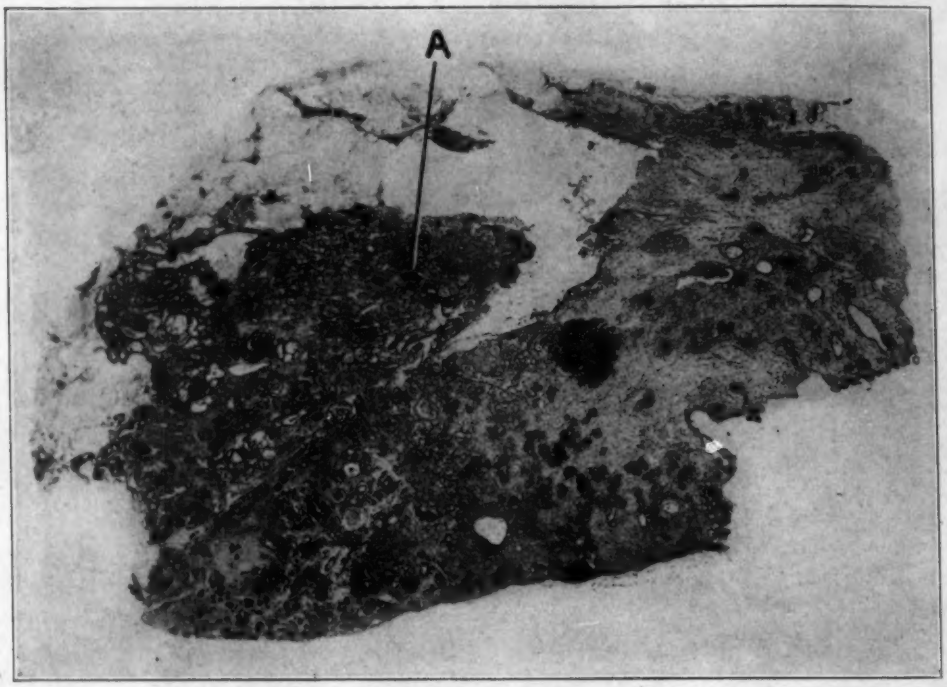

Fig. 17 (case 8).—Whole microscopic section of the breast: The diseased area is triangular with the apex of the triangle directed toward the nipple. It is composed of many small cysts which are distended by neoplastic epithelium. At *A* carcinoma is present, the epithelium of which is undergoing gelatinous degeneration.

in the axilla. The opposite breast was normal. On the basis of these clinical signs alone, radical operation was performed.

Pathologic Examination.—Figure 17 shows a vertical section of the breast that was cut in a plane parallel with the anterior surface of the body. Many small cysts full of epithelial neoplasia were visible. These cysts were ducts and acini distended by epithelial neoplasia which was not very anaplastic. Epithelial cells could be seen invading the stroma of the breast, where gelatinous degeneration was marked. Here and there, in the center of some of the cysts, epithelial cells

had undergone gelatinous degeneration to a slight degree (fig. 18). The elastica stained normally. The lymphatic glands in the axilla were free from disease.

Comment.—This specimen demonstrates the importance of localized nodularity in a breast as a sign of early carcinoma. This sign is important whether or not it is accompanied by pain. Case 8 is another example of gelatinous degeneration beginning in epithelial cells. It resembled cases 1, 2 and 3 in that the primary neoplastic epithelial change within the ducts and acini was extensive and largely confined within normal boundaries. The limitation of the carcinoma in the breast can probably be explained by the fact that the epithelial neoplasia was

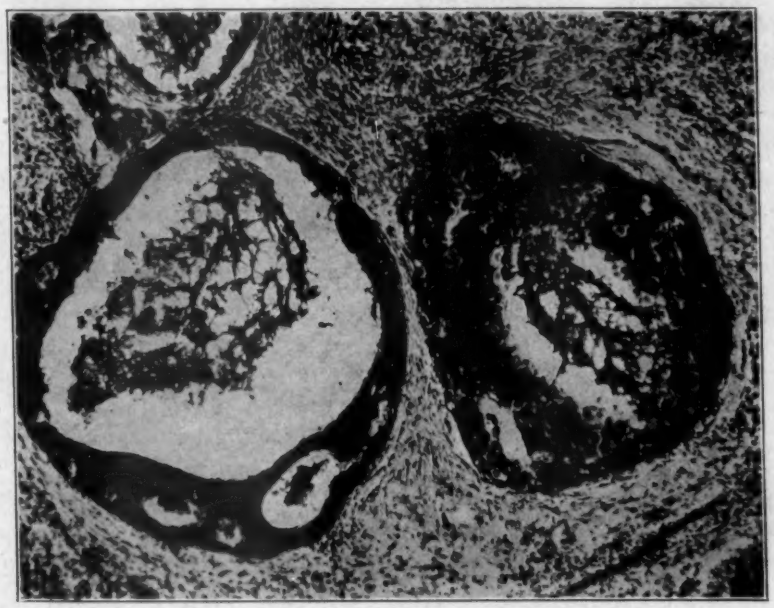

Fig. 18 (case 8).—High power view of two cysts in figure 17 showing different stages of gelatinous degeneration in the center and along the margins.

not highly anaplastic. In this specimen, the gelatinous degeneration was early and slight and might easily have been missed had it not been for the fact that whole microscopic sections were cut of the breast.

SUMMARY AND CONCLUSIONS

The study of whole microscopic sections of carcinoma of the breast in which gelatinous degeneration had occurred has led to the following conclusions:

1. Gelatinous degeneration is more common in carcinoma of the breast than is generally supposed. This conviction is based on the fact

that from a study of whole sections we have discovered gelatinous degeneration in tumors in which its presence was totally unsuspected. These observations lead us to believe that if carcinomatous breasts were always systematically examined by means of whole serial sections, the discovery of gelatinous degeneration would be more frequent.

2. The process of gelatinous degeneration begins and ends in the epithelium only. The study of specimens that show gelatinous degeneration in all stages convinces us of this fact. Moreover, the presence of gelatinous degeneration in metastatic deposits is further evidence in favor of its origin in the epithelium.

3. The areas in which gelatinous degeneration appears to have infiltrated the connective tissue stroma of the breast consist of the remains of degenerated epithelium which has disappeared completely, leaving only a gelatinous meshwork. This gelatinous degeneration begins and ends in epithelium confined within ducts and acini and also affects the epithelium that has invaded normal structures. The final stage of both events gives rise to morphologic appearances that have been interpreted as evidence of a primary gelatinous degeneration in connective tissue cells.

4. The large size of some of the tumors we have examined has been due to the wide distribution of apparently malignant epithelial neoplasia existing in ducts and acini. Whole or chief parts of a duct or even two ducts and its terminal branches and acini may be thus affected.

5. The presence of gelatinous degeneration in a carcinoma of the breast does not necessarily imply a low degree of malignancy, as is generally supposed. Four of our cases were among the most malignant that can be encountered in the breast, and in all death resulted from the disease. Morphologically, they were highly anaplastic, and clinically their high degree of malignancy was demonstrated by prompt recurrence, widespread metastasis and a rapid course.

6. The clinical course of tumors exhibiting gelatinous degeneration is determined chiefly by the precise biologic properties of the epithelial elements they contain and does not depend on either the presence or the extent of the gelatinous degeneration.

7. Carcinomas of the breast exhibiting gelatinous degeneration often possess a comparatively low degree of malignancy. On the whole, however, we believe that gelatinous degeneration is one of the secondary and adventitious changes that may occur in the course of any carcinoma and does not necessarily determine the degree of malignancy of the tumor.

GOITER

MANAGEMENT OF THE POOR SURGICAL RISK *

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Since the advent of aseptic surgery, the introduction of iodine in the preoperative preparation of patients with exophthalmic goiter has been the most momentous single advance made in the surgical treatment for diseases of the thyroid gland. Viewed either as to its revolutionary beginning or as to its far-reaching effect on the whole field of surgical treatment for the thyroid gland, the year of its discovery has opened a new era in the progress of this branch of surgery. The contrasts between the new and the old are great. In numerous articles attention has been called to the pronounced effect of the administration of iodine on the pathologic changes in the gland and on the course of the disease as evidenced particularly by the change in the symptoms and the appearance of the patient, by the lowering of the basal metabolic rate and by the absence of severe postoperative explosive reactions. This has resulted in a smoother convalescence, in a tremendous reduction in the need for ligations and operation performed in stages, and finally in a marked decrease in the operative mortality. As a consequence, surgery of the thyroid gland has been placed on a sound basis similar to that of other branches of general surgery, whereby in all but a small group of complicated cases the surgeon can confidently predict that if the operation is done expeditiously and without technical mishaps, the patient will easily endure the operation. This differs greatly from the conditions existing prior to the use of iodine, when in nearly 70 per cent of cases of exophthalmic goiter the surgeon feared the development of an unexpected postoperative reaction which was the immediate or contributory cause of death in more than 50 per cent of the fatal cases. To reduce the possibility of these reactions, ligations and operations performed in stages were resorted to at a tremendous cost in both suffering and economic waste. In only 30 per cent of the cases were conditions so favorable that the surgeon felt reasonably assured of the safety of primary subtotal thyroidectomy. Today safety has replaced the uncertainty of yesterday.

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* From the Division of Surgery, the Mayo Clinic.

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Looking back to the period before iodine was used, the frequent employment of preliminary procedures and the not infrequent unexpected fatal reactions would indicate that there were no clearcut reliable criteria of the patient's condition by which the safety of surgical procedures could be judged accurately. Although it is true that the presence of severe hyperthyroidism verging on a crisis of the disease, and the marked debility of the patient often resulting from long existing hyperthyroidism or from an associated disease were recognized as factors that would greatly increase the hazard of an operation, the fact remains that in most patients with moderate hyperthyroidism, many of whom were able to perform their daily work, there was no accurate guide to separate the good risk from the bad. In consequence of this inability to prejudge the individual hazard, the surgeon, appreciating the narrow margin of safety and sensing the many hidden pitfalls, wisely accepted nearly two thirds of the patients as uncertain or poor risks, and adjusted the entire surgical management on this basis. In order to protect such patients, any special needful treatment had to be administered also to a large group, many of whom did not actually require it. This was extravagant and, under certain circumstances, impracticable.

The introduction of iodine into the method of preparing the patient, under cooperative management, has wrought a complete change in these conditions, for no longer does the specter of death from an unexpected postoperative explosion continually confront the surgeon. With the remarkable decline in the mortality rate, the surgical treatment has been so altered that preliminary ligations have been practically abandoned and the two-stage procedures are employed only in exceptional instances in which indications are clearcut. However, excessive enthusiasm should not be permitted to impair the surgeon's critical faculties to the extent that he accepts all postoperative deaths, under the present management, as inevitable. Instead, he must search for their cause and prevention.

Are there today any recognizable factors in the patient's condition that influence the hazard of operation? In an attempt to answer this, a review was made of all the patients with exophthalmic goiter and of those with adenomatous goiter and hyperthyroidism who were operated on in the Mayo Clinic from Jan. 1, 1925, to Dec. 31, 1928, inclusive, with the idea of determining the influence on the mortality rate of age, duration of the disease and the severity of the hyperthyroidism as measured by the basal metabolic rate. Other factors, such as debility and the degree of myocardial or hepatic degeneration, which can often be detected clinically but which cannot be precisely estimated, were not considered. The simple goiter without hyperthyroidism was not included in the study, since the operative hazard in these cases is slight and the number of deaths is too small to be of any statistical value. During this

period there were 5,081 patients operated on for exophthalmic goiter and 2,171 for adenomatous goiter with hyperthyroidism. Forty-six of the former died, a mortality of 0.9 per cent, and twenty-nine of the latter died, a mortality of 1.3 per cent.

INFLUENCE OF THE DURATION OF HYPERTHYROIDISM AND AGE ON MORTALITY RATE

From the records of 1,477 cases of exophthalmic goiter, it was not possible to obtain with any degree of accuracy the probable time of the

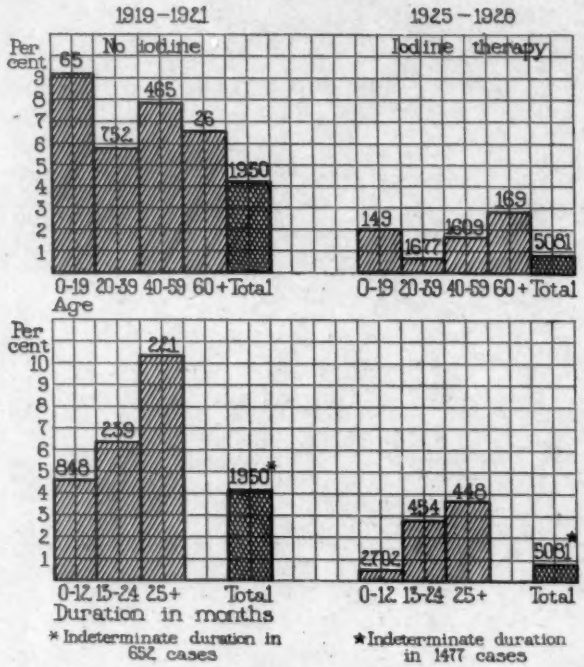

Fig. 1.—Exophthalmic goiter. The effect of age and of duration of disease on the mortality rate with and without iodine treatment.

onset of the disease. In the other 3,604 cases, the time of onset was definite and these were grouped under three headings, according to the duration in months of the hyperthyroidism. For comparison, a similar study was made of the records of all the patients with exophthalmic goiter operated on during the years 1919, 1920 and 1921, who had not been given iodine. Of the 1,950 patients, 81 died—a mortality of 4.15 per cent. In 1,308 cases the time of onset of the disease could be determined and they were grouped similarly according to the duration of the hyperthyroidism.

The marked benefit of giving iodine in surgical cases of exophthalmic goiter is seen by comparing the mortality rate in the two series (fig. 1). In both series the duration of the disease exerted a pronounced influence on the mortality rate, more marked in the later series, in which iodine had been given. This can be explained by the fact that in the early case of exophthalmic goiter there is usually only one additional operative hazard, the severity of the hyperthyroidism, while in the late case there are two, the severity of hyperthyroidism and the presence of visceral degeneration. As iodine will largely control the danger incident to the severity of the hyperthyroidism, it has eliminated the only additional surgical hazard in the early case, whereas it has removed only one of the two hazards in the late case. It is apparent, then, that the longer the patient has the disease before submitting to surgical procedures, the

Duration of Exophthalmic Goiter

Year	Average Duration of Hyperthyroidism, Months	Patients Having Hyperthyroidism for Twelve Months or Less, Per Cent
1909	31.24	45.36
1910	33.56	40.17
1911	24.62	57.60
1915	23.37	57.61
1916	23.19	63.23
1917	19.55	68.31
1918	22.57	61.82
1919	20.26	64.07
1920	19.16	65.68
1921	19.59	65.42
1922	18.31	65.81
1923	18.02	67.20
1924	21.00	69.95
1925	21.60	69.96
1926	15.90	76.37
1927	15.40	77.94
1928	14.35	75.21

greater the operative hazard. However, there is a definite trend year by year for the patient with exophthalmic goiter to seek operation sooner after the onset of the disease (table), and this is the most hopeful sign in the solution of the goiter problem.

Among patients having adenomatous goiter with hyperthyroidism, the duration of the hyperthyroidism had an equally significant influence on the mortality rate (fig. 2).

With the exception of the group of patients aged less than 20 years, the advance of years beyond 40 is an increasing factor of significance in the surgical mortality rate in cases of exophthalmic goiter. It would appear that the resistance to the disease in the young is definitely less than after full maturity. This fact has long been recognized, and for the young a longer period of preoperative preparation has been urged.

Age plays a far more prominent part in the mortality rate of patients who are suffering from adenomatous goiter with hyperthyroidism than of those who have exophthalmic goiter. One patient,

a girl aged 19, who had been an invalid for many years as the result of an attack of anterior poliomyelitis in childhood, was the only patient aged less than 20 who died. Because of great weakness, she was unable after operation to raise the mucus; the mucus accumulated and she literally drowned in her own secretions; age was in no way a factor. The greatest mortality rate occurred in patients of advanced years.

HEIGHT OF BASAL METABOLIC RATE

In the analysis of this series of cases of exophthalmic goiter, it was clearly demonstrated that the height of the basal metabolic rate

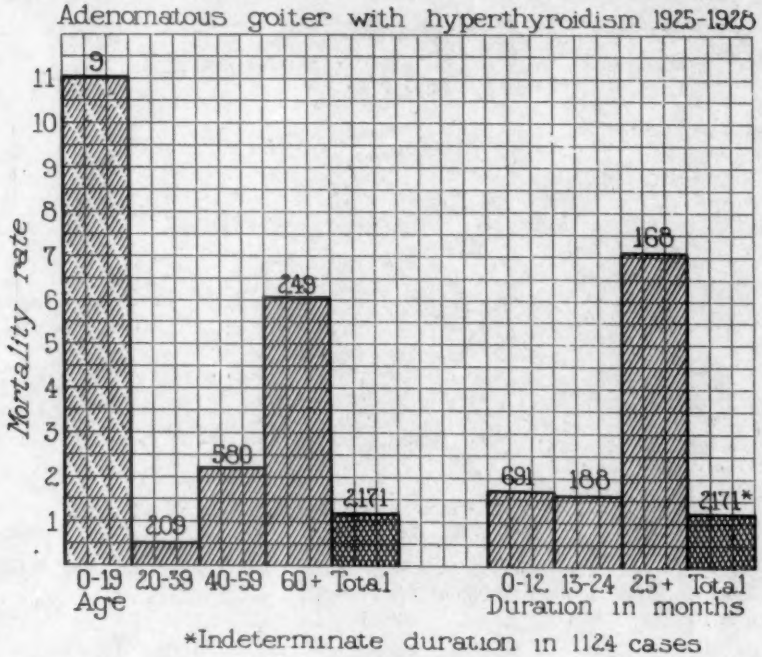

Fig. 2.—Adenomatous goiter with hyperthyroidism. The effect of age and of duration of the disease on the mortality rate.

was a significant factor in the mortality rate. Viewed as a whole, a considerably larger percentage of deaths occurred if the basal metabolic rate was more than +50 than if it was less than +50, and it would appear that the higher the rate above +75, the greater the operative hazard (fig. 3 *a*). Contrasting the two series of cases of exophthalmic goiter, it was found that twenty (1 per cent) of the patients who had been operated on without being given iodine died from a postoperative hyperthyroid reaction within twenty-four hours, whereas only seven (0.14 per cent) of those who had had iodine died in a similar manner.

It would seem that the effect of iodine was greatest on the patients with a moderate or low basal metabolic rate (fig. 3 *b*). The influence of the height of the metabolism on the surgical hazard in the cases of adenomatous goiter with hyperthyroidism is similar to that in cases of exophthalmic goiter (fig. 3 *c*).

SURGICAL HAZARDS

The increased potential hazards in surgery of toxic goiter can be conveniently divided into: (1) the development of an overwhelming postoperative hyperthyroid crisis; (2) the debility of the patient resulting from the intensity of the disease or the long continued hyperthyroidism, advanced age, or from some intercurrent disease, and (3)

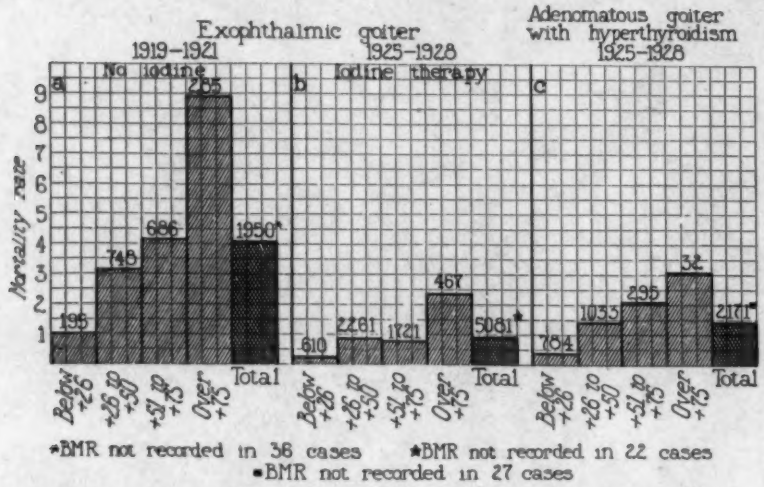

Fig. 3.—Mortality rate based on the height of the basal metabolic rate: *a*, exophthalmic goiter without iodine treatment; *b*, exophthalmic goiter with iodine treatment, and *c*, adenomatous goiter with hyperthyroidism.

increased technical difficulties occasionally met with in huge obstructive goiters. In fifty-eight of the seventy-five fatal cases in this series, necropsy was performed. The most common anatomic abnormalities were myocardial degeneration, which in five instances produced arterial emboli, pneumonia, pulmonary edema and atrophy of the liver.

Is it possible, on the basis of these potential dangers, to gage with a reasonable degree of accuracy the surgical hazard of the individual patient with goiter? To determine this a written preoperative record must be made of the individual ratings of all patients and then the mortality checked with these ratings. An attempt to carry out this plan was made on one service in the clinic. The grading of operative risks was made on the basis of 1, 2, 3 and 4. The normal risk of the

patient with goiter unassociated with hyperthyroidism was graded 1, and the normal risk of the patient with goiter associated with hyperthyrodism was graded 1+. The estimation of any additional hazard was added to the normal rating. In this series 1,486 patients with toxic goiter were operated on during the years 1927 and 1928. Eleven patients died. Of the total number, the risk in 251 cases (18 per cent) was adjudged to be moderately increased, and in fifteen cases (1 per cent)

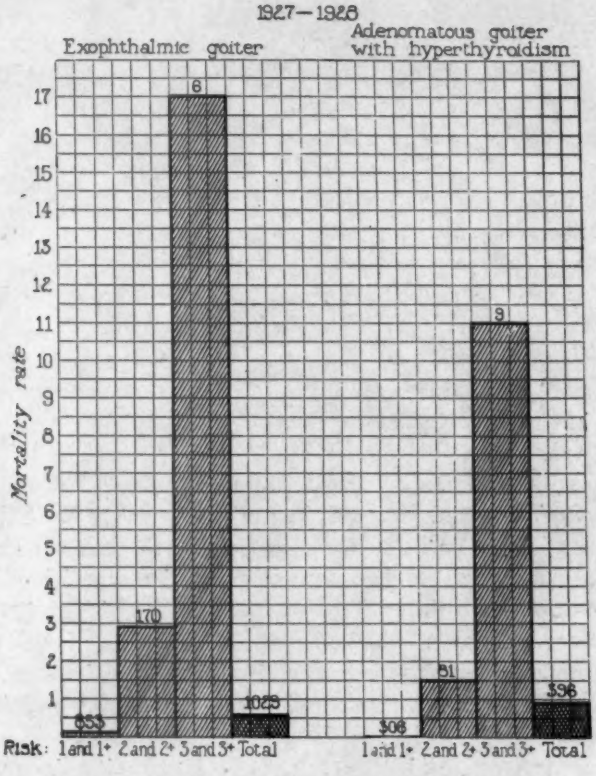

Fig. 4.—Mortality rate based on predeterminate risk.

to be greatly increased (fig. 4). Nine of the eleven patients who died were in these two groups, comprising 19 per cent of the total. It is evident that although it is not possible to foretell which patient will not survive the operation, it is possible from a clinical estimate of the hazard to select a small group (19 per cent) from which 81 per cent of the mortality will be derived.

TREATMENT

The treatment of the patient representing a poor risk is divided into three stages, preoperative, operative and postoperative, no one of which

can be considered to outrank the others in importance, as success is frequently dependent on the careful management of all three.

Preoperative Treatment.—Secondary in importance only to iodine treatment has been the organization of cooperative management of patients with toxic goiter whereby throughout the entire period of observation they are under the joint supervision of the internist and the surgeon. Under such a system the operative hazard can be more accurately estimated, the patient who is a poor risk can be prepared more intelligently and complications can be more quickly detected and efficiently managed. Iodine, a diet high in calories, and adequate rest are essential to the proper preparation for operation of all patients with exophthalmic goiter. The details of this management have been discussed frequently, and here I shall emphasize only certain additional measures necessary for the handicapped patient.

Not infrequently, patients with severe hyperthyroidism are operated on before they have been adequately prepared. This error is sometimes accounted for by an unfounded belief that the effect of iodine on the disease is transient, and that to obtain its maximal benefit the operation must be performed within the limited time of from two to three weeks. Although from eight to twelve days is sufficient time for the preparation of most patients, a considerably longer period is required by others, particularly those who on admission are greatly prostrated from acute severe hyperthyroidism. To operate on such patients before they have at least partially regained their weight and strength may prove disastrous, but a delay of three or four weeks or longer will insure an easy convalescence. Adequate rest does not necessarily imply continous confinement to bed up to the time of the operation. This is debilitating, and when a patient is thus confined he becomes a fit subject for the development of postoperative pulmonary complications. If strict confinement is necessary, as it is for patients with cardiac decompensation, it is advantageous for the patient to be up and about a part of each day, until he has recovered his strength, before operation is undertaken. In my experience, the observance of this rule has been of inestimable value.

In preparing patients with obvious cardiac disease, one is frequently tempted to administer digitalis in the hope of quieting the heart and increasing its reserve. Since 1923, however, at Plummer's suggestion digitalis has been given only occasionally, for example, to patients with cardiac decompensation when rest alone has failed to restore the compensation. The results have fully justified this policy. Deaths cannot be attributed to failure to give digitalis, and unquestionably convalescence has been smoother.

Patients with degenerative changes in the liver, as evidenced by the phenoltetrachlorphthalein retention test, and those with diabetes mellitus

may have the glycogen reserve materially increased by preoperative preparation: in the first group by the intravenous injection of 10 per cent dextrose in sodium chloride solution, and in the second by a diet high in calories and rich in carbohydrates, supplemented by adequate insulin to make possible its utilization.

Operative Treatment.—The choice and the manner of administering the anesthetic are of prime consideration in the operative treatment of the patient who is a poor risk. It is not unusual for enthusiasts to advocate some particular inhalation anesthetic as being peculiarly suitable for operations on patients with goiter. From my experience I am in thorough accord with the teachings of Crile, that the employment of prolonged inhalation anesthesia is deleterious to the handicapped patient. Local anesthesia alone is not essential, and moreover it cannot be administered successfully to many of the patients. I have found that infiltration with procaine hydrochloride supplemented by nitrous oxide and oxygen is the most satisfactory method of anesthesia. Under this method the average duration of administration of gas is from eight to ten minutes. For patients with obstructive dyspnea, local anesthesia is definitely indicated. Sodium amytal (sodium iso-amylethyl barbiturate) narcosis has been employed in the Mayo Clinic with success in many operations on the thyroid gland, but I am of the opinion that it has one disadvantage which should prevent its general use in this field. Patients are asleep during the entire operative procedure, and therefore it is not possible to test the function of the vocal cords by having the patient speak or cough. The discovery of an injured nerve during the course of the operation may be of the utmost value in its ultimate success.

Ligations.—In the period before the use of iodine, preliminary ligation of the thyroid vessels was a highly valuable and almost indispensable means of preparing for operation the patient who was a poor risk. It was used extensively, with most gratifying results. Today are there any indications for its employment? I said recently:[1]

> The benefits of polar ligation are obtained by reducing the intensity of hyperthyroidism. The group of patients who receive the greatest benefit from ligation are the same as the group in which treatment with iodine is most effective. The early case of severe hyperthyroidism, with pronounced bruit and thrill over the thyroid vessels, responds in a striking manner to ligation, but in this group iodine is even more effective. In the late cases with the hard, trained gland, iodine often apparently does not affect the course of the disease. In cases of this group in which benefit has not been derived by treatment with iodine, and in which the operative risk is considered poor on account of the intensity of the hyperthyroid-

1. Pemberton, J. deJ.: Exophthalmic Goiter: Indications for the Stage Operation, Arch. Surg. **18**:735 (Feb.) 1929.

ism, ligation should be performed as a preliminary procedure. It has been my experience, however, that if treatment with iodine fails to influence the course of the disease, ligation is equally ineffective.

In the Mayo Clinic, ligations have not been employed in the last 2,000 operations for exophthalmic goiter.

The essential technical features of the operation for goiter consist in the removal, under aseptic conditions, of excessive thyroid tissue, with the preservation of sufficient gland to maintain the basal metabolism within normal limits, with the minimal loss of blood and with the least possible trauma to the contiguous structures. In operation on the patient who is a poor risk the avoidance of technical errors is of paramount importance, for the margin of safety is so narrow that any additional complications may prove to be just sufficient dead weight to tilt the scales to the disadvantage of the patient. Theoretically the list of the possible errors would make a varied and formidable array, but actually under modern methods only two occur with a degree of frequency to be worthy of special note, namely, injury of the recurrent laryngeal nerve and postoperative hemorrhage. Both of these can be prevented only by extreme care in details. If the surgeon is in the least uncertain as to the effectiveness of the hemostasis, one of two additional steps is advisable: ligation of one or both inferior thyroid arteries at a point proximal to their entrance to the gland, or packing the cavity and leaving the wound open. I frequently adopt the former procedure (fig. 5). As I have previously pointed out,[2] the strict adherence to two principles of technic will greatly lessen the chance of injuring the nerve: the preservation of the posterior mesial portion of each lateral lobe, and the avoidance of exposure of the lateral wall of the trachea. In all cases it is highly desirable that the functional integrity of the nerve be determined by having the patient awaken and by noting the character of the voice or cough after resection of the first lobe.

In the event of injury of a nerve during the removal of the first lobe, the surgeon must be acquainted with that fact before the resection of the second lobe. Experience has proved that the immediate removal of a constricting suture unwittingly placed around the nerve will result in complete functional restoration in from six to ten weeks; on the other hand, I believe that all such sutures allowed to remain will eventually cause permanent paralysis of the nerve. If the nerve has been injured during the operation on a patient, who is a poor risk, this should be a definite indication to defer the resection of the second lobe until a later date. Likewise, if the resection of the first lobe is attended

2. Pemberton, J. deJ.: Obstructive Dyspnea Following Surgery of the Thyroid Gland and Its Prevention, S. Clin. North America 4:451, 1924.

by excessive loss of blood or undue prolongation of the operation, it is advisable to postpone the operation on the second lobe. Lobectomy may be indicated in another group of late cases of two years' standing or longer, in which the glands are large and firm and may be technically difficult to resect. Most such patients will safely tolerate uncomplicated

Fig. 5.—Methods of controlling bleeding: *a*, ligation of the branches of the individual vessels; *b*, hemostatic suture of the remnant of the gland, and *c*, ligation of the inferior thyroid artery at a point proximal to its entrance into the gland.

subtotal thyroidectomy, but would probably succumb if there were any additional burdens, such as those imposed by the occurrence of a technical error. Any modification of the operative procedure that would

improve the patient's condition at a reduced risk should be substituted for primary subtotal thyroidectomy. The operative risk of lobectomy is definitely less than that of subtotal thyroidectomy, for the surgical trauma and the chances of a technical error attendant on the former are just half those of the latter. If the patient can endure lobectomy, the resulting improvement will be so marked that the second lobe can be resected later at a greatly diminished hazard. An accident at the second stage would not necessarily prove disastrous. As a matter of record, in the Mayo Clinic, the operation in stages is now being employed in less than 1 per cent of all cases of toxic goiter.

Postoperative Treatment.—During immediate convalescence a large percentage of the patients do not require special treatment other than the symptomatic measures employed as a routine. However, it is probable that in no other field of surgery can more be accomplished in the treatment for grave complications. As already indicated, the most frequent postoperative complications are obstructive dyspnea, acute hyperthyroid reaction, and pulmonary edema and infections, and, as successful management of these is dependent on early recognition of impending signs and the prompt institution of proper treatment, close supervision by an experienced internist is indispensable. It is for this type of complications, associated with cyanosis, that oxygen treatment, particularly in the oxygen chamber, has proved to be of great value. Recently, Haines and Boothby [3] reviewed the physiologic basis of oxygen treatment and analyzed the results in the treatment for complications in 126 cases following operation on the thyroid gland. They summarized their observations as follows:

> We believe that the therapeutic administration of oxygen by means of the chamber or tent is most helpful in a restricted group of cases, such as postoperative pulmonary edema, bronchopneumonia and respiratory obstruction. The patients who show most marked benefit are those with evidence of anoxemia, or of impending anoxemia. Treatment should be begun as early as possible, as in many instances the progress of pulmonary edema to pneumonia probably can be averted. Treatment should be continuous, or as nearly continuous as possible, until the pathologic process is well controlled. . . . Treatment with oxygen can be carried out more efficiently in oxygen chambers than in oxygen tents, although excellent results can be obtained in tents properly manipulated. We do not know that the life of any individual patient has been saved by oxygen treatment; however, we believe that at least an occasional patient is saved when marked lowering of the temperature and increased comfort can be secured in such a large series of patients who are seriously ill. Our results not only warrant the continuation of this method of treatment but indicate the advisability of more general adoption of efficient methods of the administration of oxygen in those diseases

3. Haines, S. F., and Boothby, W. M.: Oxygen Treatment with Special Reference to Treatment of Complications Incident to Goiter, Am. J. Surg. **7**:174, 1929.

known to be benefited by its use. The patients who obtain the greatest benefit are those with postoperative pulmonary edema, bronchopneumonia, or respiratory obstruction accompanied by cyanosis or impending cyanosis.

SUMMARY

By contrasting the records of a large series of patients with exophthalmic goiter who were operated on after having taken iodine with a similar series of patients operated on without having taken iodine, the effect of iodine treatment was determined. The practical elimination of the need for preliminary ligations and the remarkable decrease in the mortality rate from 4.1 to 0.9 per cent are outstanding. Furthermore, by greatly reducing the incidence and severity of the postoperative reactions, the most uncertain of the operative hazards, iodine medication has made it possible to evaluate more accurately other factors that influence the surgical mortality rate. The duration and severity of the hyperthyroidism, as measured by the height of the basal metabolic rate and the age of the patient, were proved to be significant influences in the surgical hazard of all patients with toxic goiter. Other obvious factors that affect the mortality rate unfavorably are visceral degeneration and intercurrent diseases. By proper evaluation of these potential dangers, the surgeon is today enabled to predetermine with a reasonable degree of accuracy the surgical hazard of the individual patient with goiter. By means of this ability to measure the hazard, it is possible to estimate the small group of patients from which the mortality is likely to be derived, and to limit the application of any additional measures of treatment needed by the handicapped patient.

The success of the operative treatment of the patient who is a poor risk is largely dependent on the avoidance of prolonged general anesthesia and of technical errors. The indications for the employment of ligation and lobectomy are limited.

Close supervision is the watchword of the postoperative care of the handicapped patient, for much can be accomplished if complications are detected early and treated intelligently. Treatment by oxygen in the chamber or tent, if instituted early, is a valuable measure in postoperative pulmonary edema, pneumonia and respiratory obstruction.

ABSTRACT OF DISCUSSION

DR. W. I. TERRY, San Francisco: To any one who is interested in goiter surgery this paper has been of great value. I agree with Dr. Pemberton that the use of compound solution of iodine has revolutionized the treatment for exophthalmic goiter. I cannot agree with him entirely as to its use in toxic adenomas. I have not obtained any results from using it, either preoperatively or postoperatively, and I discontinued using it in those cases. But with the cases of hyperplastic thyroid, the true exophthalmic goiter, it has reduced the mortality tremendously. In the hands of any one who performs a fair number of operations for goiter, the mortality from exophthalmic goiter should not be much

more than 1 per cent. That is what we have had at our clinic since compound solution of iodine has been used. Previously, it was 3.5, and even 4, per cent. It was much higher than that at the hands of surgeons who were operating only occasionally for goiter. Dr. Pemberton did not have an opportunity to speak about the use of digitalis, but I know his views on the subject and they accord entirely with ours. We use digitalis only when there is decompensation of the heart; otherwise not many of these instances of decompensation are among the cases of toxic adenoma. In operating, it is important to preserve the lateral as well as the posterior capsule of the thyroid, with the object of conserving the parathyroids and the recurrent laryngeal nerve. This technic has been described by us elsewhere.

Dr. Thomas M. Joyce, Portland, Ore.: Symptoms and physical signs referred to the heart are sought for and expected to be found in every case of thyrotoxicosis in which other clinical symptoms of thyroid hyperplasia are met. These symptoms vary from simple tachycardia to signs of well marked congestive cardiac failure. We have not recognized a line of demarcation between the early signs of cardiovascular disease and the late signs with which comes true failure. The pathology of the heart lesion in thyrotoxicosis may not be an accepted entity; it may not be specific, although certain studies suggest a specificity.

With the presence of a widespread edema, our method of treatment begins with a Karell milk diet; after two days, the diet is changed to a low protein, and salt diet and the liquid intake is restricted to 800 cc. per day. The Minnesota-grown powdered digitalis is administered, 4 grains (0.026 Gm.) per day, until physiologic tolerance is reached. All digitalis is stopped for a period of three days before operation.

Sugar in the urine is a rather frequent complication of hyperthyroidism. When it is due to diabetes mellitus it is a serious complication and requires careful preparation of the patient for operation. On the other hand, when it can be classed as a so-called glycosuria it is of no consequence and may be disregarded. When dextrose is found in the urine of a patient suffering with hyperthyroidism, a fasting blood sugar estimation should be made. If the blood sugar during fasting proves to be within normal limits (between 80 and 120), this does not necessarily rule out diabetes, as many patients with mild diabetes present normal blood sugar while fasting. The usual interpretation of the blood sugar curve is as follows: If the blood sugar is above 160 mg. in one hour and fails to return to normal an hour later after dextrose has been given, a diagnosis of diabetes can logicaly be made. Parathyroid preservation is of great moment.

Tetany is also produced by temporary swelling of the gland, shutting off of the blood supply to the parathyroids and by calcium deficiency from persistent vomiting, loss of hydrochloric acid in the stomach and consequent alkalosis. Tetany is easily recognized and almost immediately relieved by the intravenous injection of parathormone and calcium chloride.

Bilateral injury to the recurrent laryngeal nerve is the most serious accident that can occur in surgical measures on the thyroid. Suturing of the nerves has not proved satisfactory, and the prospect of wearing a tracheotomy tube for life presents a most gloomy outlook for the patient.

Dr. C. C. Tiffin, Seattle: Dr. Pemberton stated that there are facing two grave dangers in thyroid surgery—hemorrhage, and injury to the recurrent laryngeal nerve. The exclusive use of local anesthesia in operations on the thyroid during a period of years has caused me to give special consideration to its many

advantages. The surgeon must be willing to do a little more work, but its use will minimize the dangers of injury to the recurrent laryngeal nerve. During the operation, the patient is required to talk; through the continued use of the pinching forceps preceding the use of the knife, injury to the nerve is minimized. This technic makes goiter surgery much safer. The patient will not die of "collapsed trachea," and he can speak aloud when he leaves the operating room.

The dangers of hemorrhage are minimized through the cooperation of a conscious patient. I believe that thyroid surgery, done in this way, is much less of a major procedure when it is based on the great principles of careful preparation brought to our attention by Dr. Plummer and the Mayo Clinic.

Dr. E. O. Houda, Tacoma, Wash.: It is singular that so little distinction is made in the literature between thyroid normalcy and pathology. In discussions, both are usually mixed in a maze of sophistries and paradoxes, revolving about a fetish consideration of iodine. Normalcy implies a unit of measure against which pathology is weighed. Acceptance of the present calculations found in literature relating to the quasisubstantiation of the iodine deficiency theory is a tacit admission that a critical study had not been made. Physiology has never contributed a direct answer to the cause of any pathology. In the light of normal calculations by Kendall which show that from 1 to 2 mg. of iodine per year maintains normal thyroid biologic chemistry, McClendon's normal figures in a three-day test in Minnesota which showed a calculated yearly retention of 3.65 mg. from an intake of 7.3 mg., and von Fellenberg's tests on himself which showed that he eliminated the entire intake while on the low diet of approximately 0.01 mg. per day, or 3.65 mg. per year, the theory is built on a weak foundation; since it is shown by accepted figures that the yearly excretion, through the kidneys alone, by persons with goiter who live in the dense goiter belts is in amount not only far beyond the physiologic requirement, but in many instances is that contained in a rich hypothetic diet.

There have been no reported determinations made in any district to show a physiologic deficiency of iodine. Marine states that there is yet an ultimate undetermined factor with which the peccancy of the goitrous gland must be connected.

Available statistics show that only an excessive intake of iodine reduces the incidence of the disease.

Bacteriology holds the key to the solution of goiter. On the observations in a consecutive series of more than 500 specimens collected in the Puget Sound district, it is stated that endemic goiter is caused by a facultative anaerobic coccus, which fails to be identified with classified bacteria.

The good accomplished by iodine, which invariably is given in massive doses when compared with physiologic needs, is unquestionably due to an alterative effect on the ultimate cause, whereas its occasional evil effects in the precipitation of toxic symptoms are due to a consequentially improved functional capacity of the multiplied cells, and an obviously increased thyroid secretion.

The toxic types of goiter are due to and synchronous with an active infectious process which is centralized in the thyroid, by selective action, but not limited to it, its metastatic dissemination being the basis of secondary organic pathology in other parts. Antigen made from cultures is specific for the infection causing endemic goiter. Preoperative detoxication is effected without therapeutic administration of iodine, and postoperative autogenous antigen effects an early and complete dissipation of residual symptoms. Surgery is a necessary factor in the established and irreversibly fixed goiters, but subtotal thyroidectomy with antigen treatment is a needless sacrifice of important tissues.

DR. J. EARL ELSE, Portland, Ore.: Many patients with goiter cannot take compound solution of iodine. They vomit. It cannot be given by rectum, because it is purging. Dextrose given intravenously will stop this crisis almost immediately because it is due to acidosis. The toxic goiter in pregnancy causes a great deal of anxiety. Some observers advise that the uterus be emptied. In my judgment, there is never any indication to induce an abortion in these cases. In the early months of pregnanacy, with the proper treatment for the goiter the majority of patients can be operated on and go to term, without a miscarriage. In the later months of pregnancy, we advise the use of roentgen rays; it is the only instance when we use the roentgen rays in the treatment for goiter. With the use of roentgen rays these patients can be cared for through confinement and be operated on about six weeks later.

We have had two deaths from tracheal collapse. I do not believe that we should have them; we consider it our fault. In the very large, diffuse adenomatous goiters, pressure on the trachea results in a weakening of the tracheal rings, so that they will collapse if the entire thyroid is removed at once. When we see these cases now, and we do not see them often, we remove only one side of the gland, wait from six weeks to two months and then remove the other side. In one patient whom I saw, after removing the second lobe a tracheal collapse occurred as a result of removing the entire goiter at one time; we therefore adopted the stage operation. It is about the only instance in which we find an indication for stage operation. I am under the impression that tracheal collapse can be prevented. It must be remembered that one operates not merely to remove the goiter at the time, but to make the patient well thereafter. In experimental work on animals, we found that regeneration of the thyroid was normally completed in a period of from three to four weeks, if the dogs were given iodine after the operation. If iodine was not given, sometimes the hyperplasia became excessive. Iodine should be given, therefore, during the regenerative period after the operation.

DR. J. DEJ. PEMBERTON, Rochester, Minn.: I am in thorough accord with everything that Dr. King said.

THORACIC SYMPATHETIC CARDIAC NERVES IN MAN

THEIR RELATION TO CERVICAL SYMPATHETIC GANGLIONECTOMY *

ALBERT KUNTZ, PH.D., M.D.
AND
ALBERT MOREHOUSE, A.B.
ST. LOUIS

The application of surgery involving extirpation of the inferior cervical sympathetic ganglions, particularly in the treatment of patients with diseases involving the blood vessels of the upper extremities, has revived interest in the anatomic relationships of the sympathetic cardiac nerves and necessitated a reinvestigation of the exact sources and distribution of these nerves.

Although Valentin [1] described nerves that arise from the medial aspect of the second thoracic sympathetic ganglion in man, extend medianward and downward, and send some fibers into the cardiac plexus, the more recent accounts of the innervation of the heart in man and in lower mammals, with few exceptions, make no mention of cardiac nerves arising from the sympathetic trunks below the inferior cervical ganglion. According to the current textbook statements, the sympathetic innervation of the heart is mediated solely through the superior, middle and inferior sympathetic cardiac nerves, which arise from the superior, middle and inferior cervical sympathetic ganglions, respectively. On the basis of this teaching, it has been regarded by some as unsafe to extirpate the inferior cervical sympathetic ganglion bilaterally, since this procedure would interrupt all cardiac accelerator fibers.

The existence of cardiac accelerator nerves arising from thoracic segments of the sympathetic trunks is indicated by both clinical and experimental data. Thoracic cardiac nerves also have recently been described, in man and in lower mammals. Perman [2] traced nerves arising from the third to the sixth thoracic ganglions into the cardiac plexus in certain *Artiodactyla* (the calf and the lamb). He was also able, in a few instances, to trace nerves from the second thoracic sympathetic ganglion to the heart in man, but concluded that no cardiac nerves arise from the sympathetic trunk in man below the second thoracic segment.

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* From the St. Louis University School of Medicine.

1. Valentin: Traité de neurologie, Paris, 1843.

2. Perman, E.: Anatomische Untersuchungen über die Herznerven bei den höheren Säugetieren und beim Menschen, Ztschr. f. Anat. u. Entwg. **71**:382, 1924.

Cannon, Lewis and Britton [3] were able to trace nerves from the medial aspects of the first three or four ganglions below the stellate ganglion on both sides in nearly all of the cats that they examined. Occasionally they could also trace nerves medianward from the fifth and sixth thoracic ganglions. They succeeded only poorly in tracing any of these nerves to the heart, but the physiologic evidence of the existence of thoracic cardiac nerves that they obtained is convincing. Dresbach and Waddell [4] claimed to have traced nerves from the sympathetic trunk as low as the fifth thoracic segment into the cardiac plexus in the cat. Reigele,[5] who studied the innervation of the heart in apes, described rami that arise from the sympathetic trunk in the upper three thoracic segments and unite to form a single nerve that joins the middle cervical sympathetic cardiac nerve on the left and the vagus on the right side. He also described a cardiac nerve arising from the fourth thoracic sympathetic ganglion on both sides. According to Jonesco and Enachescu,[6] who described thoracic sympathetic cardiac nerves in the cat, dog, calf, sheep and man, these nerves are best developed in *Artiodactyla* and man. On the basis of their observations in human fetuses and two adult cadavers, they concluded that the thoracic cardiac nerves are constant in man and usually occur bilaterally. According to their observations, these nerves arise mainly from the ganglions or intervening portions of the sympathetic trunk in the second to the fifth thoracic segments. They commonly anastomose with each other and with the inferior cervical sympathetic cardiac nerve and cardiac branches of the vagus.

Our study of the thoracic sympathetic cardiac nerves in man is based on adult and young cadavers and on stillborn fetuses. The following description of the nerves is based mainly on our observations on adult cadavers. The cardiac plexuses and the intercommunications of the nerves entering them remain relatively simple in the fetus. It is possible, therefore, to trace individual nerves and their branches nearer to their terminations in relation to the heart than in the adult, but the smaller nerves entering the cardiac plexus are so delicate in the fetus

3. Cannon, W. B.; Lewis, J. T., and Britton, S. W.: A Lasting Preparation of the Denervated Heart for Detecting Internal Secretion, with Evidence for Accessory Accelerator Fibers from the Thoracic Sympathetic Chain, Am. J. Physiol. **77**:326, 1926.

4. Dresbach, M., and Waddell, K. C.: K-Strophanthidin Emesis in Cats with Denervated Hearts, J. Pharmacol. & Exper. Therap. **27**:9, 1926.

5. Riegele, L.: Ueber die Innervation der Halz- und Brustorgane bei einem Affen, Ztschr. f. Anat. u. Entwg. **80**:777, 1926.

6. Jonesco, D., and Enachescu, M.: Untersuchungen bei Säugetieren und beim Menschen über die aus dem Brustgrenztrang Unterhalb des Ganglion stellatum entspringenden Herznerven, Ztschr. f. d. ges. Anat. **85**:476, 1928.

that they can be traced only with the greatest difficulty. We have, therefore, preferred to describe the thoracic cardiac nerves in the adult cadaver, although it is impossible by dissection to determine the exact distribution of any given nerve within the cardiac plexus.

In all the cadavers examined, a nerve could be traced from the medial aspect of both the second and the third ganglion of the sympathetic trunk below the inferior cervical ganglion or from the interganglionic portions of the sympathetic trunk in the second and third thoracic

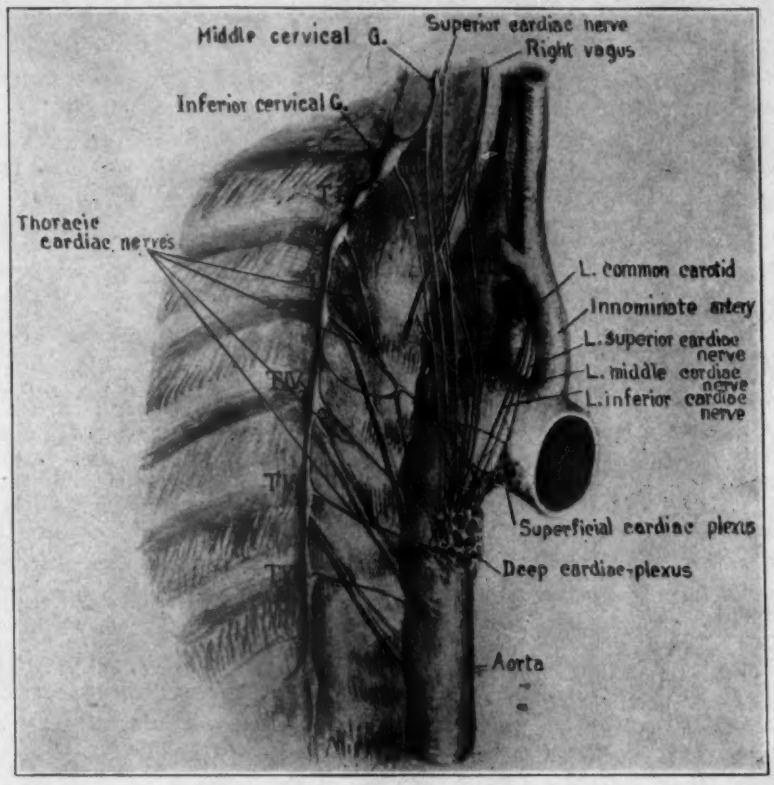

Fig. 1.—A drawing from a dissection of a human cadaver illustrating the nerves entering the cardiac plexus from the right side.

segments. These nerves commonly unite, forming a single trunk which tends medianward and downward and gives rise to branches, some of which join one or more of the cervical sympathetic cardiac nerves and cardiac branches of the vagi; others enter the deep cardiac plexus directly. In some instances, a branch could also be traced into the superficial cardiac plexus. This branch occasionally joins the superior cardiac nerve on the left side. In many instances, a ramus arising from the fourth thoracic ganglion also joins this nerve. On the right side,

it passes posterior to the esophagus and approaches the deep cardiac plexus between the esophagus and the lateral aspect of the aorta. It also sends a few small branches into the right pulmonary plexus. On the left side, it passes posterior to the aorta and approaches the deep cardiac plexus from the right side. One or more branches of this nerve often anastomose with branches of the corresponding nerve on the right side before the latter joins the cardiac plexus. A nerve also arises from the fourth thoracic ganglion of the sympathetic trunk which, on the right side, can be traced directly into the deep cardiac plexus. On the left side, the nerve passes posterior to the aorta and joins the deep cardiac plexus from the right side. These nerves also supply slender branches to the pulmonary and esophageal plexuses, particularly on the right side. In the majority of the cadavers examined, slender nerves could also be traced from the fifth and sixth thoracic ganglions of the sympathetic trunk toward the aorta bilaterally. In some instances, branches of the nerve arising from the fifth thoracic ganglion on the right side could be traced into the deep cardiac plexus. Other branches became incorporated in the plexus on the descending aorta. In no case could branches of nerves arising from the sympathetic trunk below the fifth thoracic ganglion be traced into the cardiac plexus. The possibility that components of the nerves arising from the fifth and sixth thoracic ganglions of the sympathetic trunks may reach the deep cardiac plexus on the descending aorta, however, is not precluded.

Clinical and experimental data strongly suggest that the cardiac nerves that arise from ganglions of the sympathetic trunk below the inferior cervical ganglion, like the one arising from the latter ganglion, convey both sympathetic and visceral afferent fibers. The sympathetic components of these nerves are at least in part cardiac accelerators. Cannon, Lewis and Britton [8] were able to elicit reflex cardiac acceleration in the cat, following bilateral extirpation of the inferior cervical and first thoracic ganglions and exclusion of all humoral cardiac accelerators, until the upper six or seven thoracic segments were removed on both sides. Bilateral extirpation of the upper three or four thoracic segments of the sympathetic trunk, following removal of the inferior cervical sympathetic ganglions, in their experiments did not completely abolish reflex cardiac acceleration. Adson and Brown [7] also reported reflex cardiac acceleration in patients following bilateral extirpation of the inferior cervical and the first and second thoracic ganglions.

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7. Adson, A. W., and Brown, G. E.: Successful Surgical Treatment of a Case of Raynaud's Disease of the Upper Extremities by Dorsal Ganglionectomy, Proc. Staff Meet., Mayo Clin. **3**:266, 1928.

According to Jonesco, Enachescu and Teitel,[8] stimulation of the peripheral ends of the thoracic cardiac nerves following section elicits acceleration of the heart rate and augmentation of the force of cardiac contraction. Stimulation of the central ends of these nerves elicits vascular reflexes, changes in the cardiac rhythm and pain. Mechanical and chemical stimulation of the heart and aorta, in their experiments,

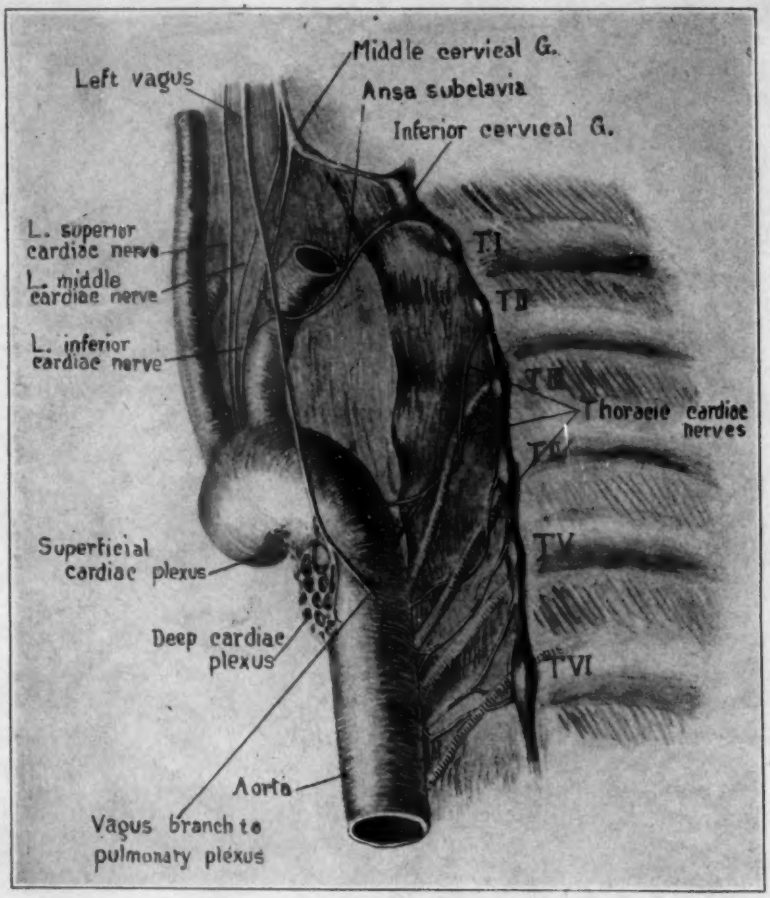

Fig. 2.—A drawing from a dissection of a human cadaver illustrating nerves entering the cardiac plexus from the left side.

resulted in pain reactions following section of all the afferent fibers that pass through the inferior cervical and first thoracic ganglions. The same stimulation did not elicit pain reactions following section of

8. Jonesco, D.; Enachescu, M., and Teitel, A. B.: Ueber eine neue Gruppe von Sympathischen aus dem Brustgrenzstrang Unterhalb des Ganglion stellatum entspringenden Herznerven, Klin. Wchnschr. **7**:991, 1928.

thoracic cardiac nerves in addition to bilateral extirpation of the inferior cervical and the first thoracic sympathetic ganglions.

The thoracic cardiac nerves are made up mainly of postganglionic fibers that arise from neurons in the ganglions of the sympathetic trunk. The existence of medullated fibers comparable in caliber to the visceral afferent components of the inferior cervical sympathetic cardiac nerve corroborates the experimental data cited which indicate that the thoracic cardiac nerves also convey afferent impulses from the heart.

Osmic acid preparations of the thoracic cardiac nerves obtained at autopsy in a child 8 months of age show that these nerves are made

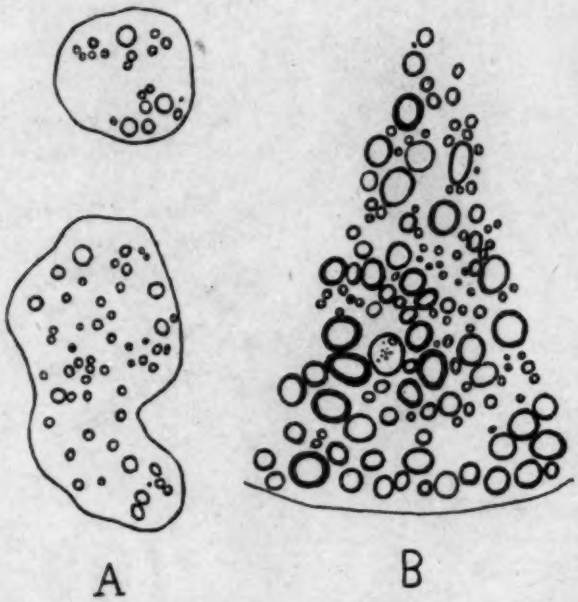

Fig. 3.—Camera lucida drawings of cross-sections of osmic acid preparations of nerves, illustrating distribution and relative size of myelinated fibers. *A*, thoracic cardiac nerves; *B*, sector of the dorsal root of third thoracic spinal nerve.

up mainly of unmyelinated fibers. They also contain myelinated fibers, some of which are equal in caliber to the largest myelinated fibers in the cardiac nerve that arises from the inferior cervical sympathetic ganglion. The larger fibers, doubtless, are general visceral afferent fibers supplying the heart.

Figure 3 represents camera lucida drawings of equal magnification of the myelinated fibers in cross-sections of thoracic cardiac nerves and a sector of the dorsal root of one of the corresponding spinal nerves in a dog. The thoracic cardiac nerves, as illustrated in figure 3*A*, con-

tain myelinated fibers of small and medium caliber. The smaller myelinated fibers in these nerves, like the unmyelinated fibers in them, probably are sympathetic. The larger myelinated fibers are definitely larger than the smallest myelinated fibers in the dorsal roots of the corresponding spinal nerves (fig. 3*B*). Since the preganlionic fibers involved in the innervation of the heart do not extend beyond the sympathetic trunk, and since myelinated postganglionic fibers are mainly fibers of small caliber, the larger myelinated fibers in the thoracic nerves, like the corresponding fibers in the inferior cervical sympathetic cardiac nerves, probably must be regarded as general visceral afferent fibers.

From our observations, it may be assumed that a certain percentage of both the cardiac accelerator fibers and the general visceral afferent components of the cardiac nerves remain intact following bilateral extirpation of the inferior cervical sympathetic ganglion or extirpation of this ganglion together with the first and second thoracic segments of the sympathetic trunk. More complete knowledge of the effect of extirpation of the inferior cervical sympathetic ganglions or section of the cervical sympathetic cardiac nerves on cardiac function awaits further investigation.

NEUROPATHIES OF THE BONES AND JOINTS

REPORT OF A CASE OF AN ARTHROPATHY OF THE ANKLE DUE TO A PERIPHERAL NERVE LESION *

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A review of the literature has revealed no complete classification of the neuropathic lesions of the bones and joints. Turney [1] has given the most detailed account of these abnormalities. Chipault,[2] Goodhart,[3] Albee [4] and others have mentioned the different conditions in which the lesions occur, but there is no agreement as to the etiologic grouping. Hence the following classification, based on etiologic factors, is presented.

1. Tabes Dorsalis
2. Syringomyelia
3. Following Lesions of the Peripheral Nerves
   - (*a*) Injury
   - (*b*) Peripheral neuritis
   - (*c*) Leprosy
4. Following Lesions of the Spinal Cord
   - (*a*) Injury
   - (*b*) Congenital malformations
   - (*c*) Tumors
   - (*d*) Tuberculosis of the spine
   - (*e*) Acute myelitis
   - (*f*) Anterior poliomyelitis
   - (*g*) Progressive (central) muscular atrophy
     - (1) Aran-Duchenne type
     - (2) Spastic type (amyotrophic lateral sclerosis)
5. Following Lesions of the Cerebrum
   - (*a*) Dementia paralytica
   - (*b*) Hemiplegia following cerebral hemorrhage.

The first two groups, tabes dorsalis and syringomyelia, are so common compared with the others that they are given separate headings. These might be included under lesions of the spinal cord.

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1. Turney, H. C.: Neurotrophic Affections of Bones and Joints, in Allbutt, Clifford, and Rolleston, Humphry Davy: System of Medicine, New York, The Macmillan Company, 1910, vol. 7.

2. Chipault, A.: L'etat actuel de la chirurgie nerveuse, **1**:142, 1902.

3. Goodhart, S. Philip: Vasomotor and Trophic Neuroses, in Tice, Frederick: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1920.

4. Albee, F. H.: Orthopedic and Reconstruction Surgery, Philadelphia, W. B. Saunders Company, 1921.

Charcot [5] was the first to describe the arthropathies associated with tabes dorsalis. He presented four cases in which there appeared suddenly a firm, painless swelling that extended to the surrounding soft parts, and in which there apparently was no preceding trauma. The rapid changes which occurred in the surfaces of the joints gave rise to luxations and false positions of the bones shortly after the onset. Because of this early, accurate description of these arthropathies, these conditions, whether associated with tabes or not, have often taken the name of Charcot joints. Allbutt [6] was the first to describe this condition in English, being followed shortly by Buzzard [7] and Thompson.[8]

Schultze and Kahler [9] (1888) were the first to describe the changes of the joints in syringomyelia similar to those found by Charcot in tabes. Schlesinger,[10] who has collected and reported 150 cases, has given the most complete account of these joints in syringomyelia. He has shown that whereas in tabes the lower extremity is more often affected, in syringomyelia it is the upper extremity.

The first instance of changes in the joints following injury to the peripheral nerves was reported by Packard; [11] arthropathies of the foot and the knee followed compression of the sciatic nerve by a tumor. Weir Mitchell [12] reported a case in which, following an injury to the brachial plexus due to a dislocation of the shoulder, extensive joint lesions developed. He added further that wounds or any lesions of nerves may produce in the joints inflammatory conditions, usually subacute, which so precisely resemble rheumatic arthritis in their symptoms and results that no clinical skill can discriminate between the two. Mitchell [13] gave the first description of the spontaneous fractures which sometimes occur in tabes dorsalis. Chipault [14] found a destructive

5. Charcot, J. M.: Sur quelques arthropathies qui paraissant d'ependre d'une lesion du cerveau on de la moelle epiniere, Arch. de physiol. norm. et path. **1**:161, 1868.

6. Allbutt, Sir Clifford: Remarks on a Case of Locomotor Ataxy with Hydrarthrosis, St. George's Hosp. Rep. **4**:259, 1869.

7. Buzzard, T.: Progressive Locomotor Ataxy with Anomalous Joint Affection, Lancet **2**:261, 1874.

8. Thompson: Case of Asynergia with Arthropathy, M. Times & Gaz. **2**: 151, 1877.

9. Schultze, F., and Kahler, O., quoted from Leede, C. S.: Arthropathien bei Syringomyelie, Munich, 1908.

10. Schlesinger, H.: Die Syringomyelia, ed. 2, Leipzig, 1902, pp. 93-140.

11. Packard, quoted by Mitchell, S. W.: Tr. Path. Soc. Phila., October, 1863.

12. Mitchell, S. Weir: Injuries of Nerves and Their Consequences, Philadelphia, J. B. Lippincott Company, 1872.

13. Mitchell, S. Weir: The Influence of Rest on Locomotor Ataxy, Am. J. M. Sc. **66**:113, 1873.

14. Chipault, A.: Arthropathies nerveuses, arthrites seches corps étrangers articulaires traite de chirurgie clinique et operatoire, Paris, Le Dentu et Delbet, 1896, vol. 3, p. 435.

arthritis of the elbow in a patient whose brachial plexus was compressed by callus formed in connection with a broken clavicle.

Bowlby [15] cited cases of Blum, Ogle and Arnozan, in which there were changes in the bone following nerve injuries. The chief alteration, however, seemed to be a simple atrophy of the osseous tissue such as might result from disuse. Bowlby stated that he had seen no cases and concluded that they are of rare occurrence. Hirsch [16] described a case of atrophy of the bone following an injury to the median nerve of the arm. Goldscheider [17] reported a case of atrophy of the bones of the hand following disease of the ulna nerve. Fleishhauer [18] cited a case of atrophy of the bones of the foot which developed three months after a traumatic neuritis of the peroneal nerve. Maliwa [19] reported several cases of atrophy of the bones of the hands, especially the phalanges, following nerve injuries. Lehmann [20] described six cases of atrophy of the bones of the hands following nerve injuries, and two cases of atrophy in the os calcis following injury to the sciatic nerve. Campbell [21] observed a case of atrophy of the bones of the foot, following an injury to the posterial tibial nerve. Nonne [22] has observed atrophy of bones within four weeks after a nerve lesion, while Köhler [23] has described it as often occurring within eight weeks after injury to the nerve.

McArdle [24] stated that he has seen arthritic changes when a nerve trunk has been pierced, rubbed or lacerated. These changes have never been seen when a peripheral nerve has been severed unless the nerve ends became bulbous or were caught in healing tissue.

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15. Bowlby, A. A.: Some Trophic Lesions Following Injuries of Nerves, Illus. Med. News **4**:25, 1889.

16. Hirsch, Karl: Ueber einem Fall von Medianusverletzung mit seltenen trophischen Störungen, Deutsche med. Wchnschr. **32**:799 and 837, 1906.

17. Goldscheider: Ueber neurotische Knochenatrophie und die frageder trophischen Funktionen des Nervensystems, Ztschr. f. klin. Med. **60**:1, 1906.

18. Fleishhauer, Kurt: Ueber Nervenverletzungen, Berl. klin. Wchnschr. **52**: 213 (March) 1915.

19. Maliwa, Edmund: Trophische Störungen nach Verletzung peripherer Nerven mit besonderer Berucksichtigung der Knochenatrophie, Med. Klin. **26** and **27**:704 and 733, 1917.

20. Lehmann, Walter: Beitrage zur Kenntnis der sekretorischen und vasomotorischtrophischen Störungen nach Nervenschussen, Med. Klin. **23**:629 (June) 1917.

21. Campbell, Harry: The Trophic Lesions, Oxford Medicine, New York, Oxford University Press, 1921, vol. 6, p. 821.

22. Nonne, M., discussion of Sudeck: Neurol. Centralbl. **21**:376, 1902.

23. Köhler: Fortschr. a. d. Geb. d. Röntgenstrhle. **12**:41, 1905.

24. McArdle, J. B.: Joint Troubles Arising from Nerve Diseases, Practitioner **45**:174, 1915.

Duncan [25] reported a case of neuropathic arthropathy of the wrist following a peripheral nerve injury. Four years prior to examination a log had fallen on the right shoulder of the patient. In the interim there had been persistent pain in the right arm, which the patient had thought to be rheumatism. Duncan believed that the original injury to the shoulder had torn some of the lower cervical and upper thoracic nerve roots. The motor roots apparently were unaffected, for the patient had no impairment in the use of the arm.

Philips and Rosenheck [26] reported two cases of neuropathic arthropathy of the shoulder due to peripheral nerve lesions. The first patient carried heavy blocks of ice on his shoulder; this prolonged muscular strain was thought to be the causative factor. The second patient, who carried timbers in his laboring work, was injured by one of these falling on his shoulder, and he was unable to return to work for ten months. The roentgenograms in both of these cases showed the changes typical of Charcot joints.

Henderson [27] stated that arthropathies of this character are not found in peripheral neuritis, except in those forms closely related to tabes. Campbell [21] has written that the neuropathic joints are rare in peripheral neuritis. Teissier [28] described a case of neuropathic arthropathy which he believed was undoubtedly of the same nature as a Charcot joint occurring in lead poisoning. A sclerosis of the cord was present, but peripheral neuritis, which doubtless existed, was not mentioned.

Potter [29] wrote that changes in the bones are frequent with leprosy and referred to a case of Harbitz, in which the phalanges were largely destroyed. Campbell [21] said that changes in the bone may occur in leprosy. Henderson [27] stated that these conditions are not found in leprosy when there is a degeneration of the peripheral nerves. Turney [1] said that the weight of evidence is in favor of Charcot's arthropathies occurring in leprosy, and that this is the only disease of the peripheral nerves in which it is found. He further added that the explanation of this lies in the extreme chronicity of the disease associated with analgesia

25. Duncan, J. H.: Neuropathic Arthritis, J. A. M. A. **79**:1987 (Dec. 9) 1922.

26. Philips, H. B., and Rosenheck, C.: Neuro-Arthropathies: A Consideration of the Etiology and General Characteristics with Especial Reference to that Form Caused by Peripheral Nerve Disease or Injury, J. A. M. A. **82**:27 (Jan. 5) 1924; Neuro-Arthropathies of Peripheral Nerve Injury Origin: Two Cases, ibid. **86**: 169 (Jan. 16) 1926.

27. Henderson, V. E.: Joint Affections in Tabes Dorsalis, J. Path. & Bact. **10**:211, 1904-1905.

28. Teissier, M. J.: Lyon méd. **54**:193, 1887.

29. Potter, H. E.: X-Ray Findings in Neuropathic Joints, J. Nerv. & Ment. Dis. **45**:449, 1917.

of the deep tissues, which is combined with unimpaired muscular power, precisely as in tabes or syringomyelia.

J. K. Mitchell, Jr.,[30] at the close of the Civil War, called attention to the influence of the nervous system on joint lesions, and reported several cases in which neuropathic arthropathies developed after injuries to the spinal cord as a result of gunshot wounds of the spine. Riedel's [31] case is the one most frequently cited to exemplify these joint lesions after injury to the spinal cord. The patient suffered a stab wound between the first and second lumbar vertebrae. This was followed by a paralysis and loss of sensation in one of the legs. Soon after the return of power to some degree, the patient tried to go about and developed an arthropathy of the knee joint. He was able to walk on the leg eight days after the injury. Charcot [32] mentioned the development of these lesions in injuries of the spine, as did Chipault.[14] Albee [4] described these joint lesions occurring after crushing injuries to the cord. Steindler [33] said that in rare instances these joints follow injuries of the spinal cord.

Hildebrand [34] reported the case of a patient with a congenital malformation of the spine, namely, a spina bifida occulta, who developed arthropathic changes. Steindler [33] stated that in rare instances these arthropathies may be associated with malformations of the spine, but failed to state whether or not these are congenital.

Chipault [2] mentioned tumors of the cord and meninges as a possible cause of neuropathic arthropathies. Albee [4] included tumors of the cord in his classification of these conditions.

J. K. Mitchell [35] was the first to describe the development of these joint lesions following tuberculosis of the spine. He reported four cases in which arthropathies developed below the point at which the spine was affected. This was the first conception of trophic centers controlling the nutrition of bones and joints and antedates by thirty-

30. Mitchell, J. K., Jr.: Remote Consequences of Injuries of Nerves, and Their Treatment. An Examination of the Present Condition of Wounds Received 1863-1865, with Additional Illustrative Cases, Philadelphia, Lea Brothers & Company, 1895.

31. Riedel, B.: Nervenverletzung der linken unteren Extremität; rapide destruction des linken Kniegelenkes durch Gehversuche, Berl. klin. Wchnschr. **20:** 252, 1883.

32. Charcot, J. M.: Leçons sur les maladies des systemes nerveux, 1883, p. 111.

33. Steindler, A.: Charcot Joints, Journal-Lancet **47:**493 (Nov.) 1927.

34. Hildebrand, O.: Ueber neuropathische Gelenkerkrankungen, Arch. f. klin. Chir. **115:**443 (March) 1921.

35. Mitchell, J. K.: On a New Practice in Acute and Chronic Rheumatism, Am. J. M. Sc. **8:**55, 1831.

seven years Charcot's description of these joints in tabes. Gull [36] (1858) reported a case of an arthropathy of the right knee following tuberculosis of the cervical spine. This has been mentioned as one of the causes of these joints by Charcot,[32] Turney,[1] Goodhart,[3] Chipault [2] and Albee.[4]

Magnier [37] described these joints in acute myelitis. This cause has also been mentioned by Goodhart [3] and Albee.[4]

Turney [1] said that these joints are found comparatively rarely in anterior poliomyelitis. He further added that the atypical cases of anterior poliomyelitis, which present all gradations up to transverse myelitis, are the ones most likely to show these bony changes. Nonne recorded a case of marked atrophy of the bones of the foot and tibia four weeks after the onset of the disease, in a boy aged 10. The anterior tibial and peroneal nerves were the ones most affected. Goodhart and Albee have given this condition as one of the causes of neuropathic lesions of the joints and bones.

Turney [1] and Goodhart [3] described these joints in progressive muscular atrophy and amyotrophic lateral sclerosis. Osler [38] considered the latter disease to be the spastic type of progressive (central) muscular atrophy. Nonne [22] recorded two cases of osseous atrophy in chronic poliomyelitis, which condition is generally accepted to be the Aran-Duchenne type of progressive (central) muscular atrophy.

Dementia paralytica has been mentioned by Barker [39] as a causative factor in these bone and joint lesions.

Hemiplegia following cerebral hemorrhage was first mentioned as a cause for arthritis by Scott Alison.[40] Dejerine and Theohari [41] described a hemiplegic patient who developed a neuropathy of the bones. Campbell [21] said that the shoulder joint is the most often affected in these hemiplegic patients, who show changes in the bones and joints. Albee [4] included this in his classification.

Turney [1] and Albee [4] grouped the neurotrophic lesions of bones and joints into: (1) osteopathies, (2) arthropathies and (3) osteo-arthropathies.

The osteopathies include the spontaneous, painless fractures. The changes are increase in the size of the medullary canal, decrease in the

36. Gull, Sir W.: Guy's Hosp. Rep. **4**:206, 1858.

37. Magnier, quoted from Turney, 1859.

38. Osler, Sir William: The Principles and Practice of Medicine, ed. 8, New York, D. Appleton and Company, 1919.

39. Barker, L. F.: Joint Affections in Nervous Diseases, J. A. M. A. **48**:384 (Feb. 2) 1907.

40. Alison, Scott, quoted from Turney: Lancet, 1847.

41. Dejerine and Theohari: Sur l'atrophie des os du cote paralyse dans l'hemiplegie de l'adulte, Compt. rend. Soc. de biol. **5**:203, 1898.

thickness of the compact bone and diminution of the lime salts. Occasionally union of the fracture takes place under the shelter of an enormous amount of callus, and then gives way without apparent cause, except the absorption of the new material.

The arthropathies appear most often in the joints which have been previously damaged, in which a slight injury will precipitate an attack. The changes may be atrophic or hypertrophic. In the ball and socket joints, such as the hip and the shoulder, the atrophic factor predominates, whereas in the hinge joints such as the knee and the elbow, the hypertrophic factor predominates. In tabes, joint symptoms occur in from 3 to 4 per cent of the patients, while in syringomyelia they are present in from 10 to 40 per cent of the cases. Of the tabetic arthropathies, the lower extremities are affected in 75 per cent of the patients, while in those due to syringomyelia, the upper extremities are affected in 80 per cent of the cases. Albee [4] has stated that in the hypertrophic type the articular cartilage disappears leaving bare the porous, cancellous bone with a few peripheral bony outgrowths in some cases. The ligaments and capsule are relaxed and distended with clear fluid. The synovial membrane is either thickened or partially destroyed together with the internal lateral ligaments.

The osteo-arthropathies most often involve the spine and the feet. In the spine the most usual lesions are kyphosis, scoliosis and spontaneous fractures. In tabes the lumbar spine is most often affected, while in syringomyelia it is the cervicodorsal spine; the feet may be flat, deviated outward or inward, or the arches may be raised.

Potter [29] has given an excellent description of the changes shown in the roentgenograms of these joints. The bone margin is irregular, spongy and fringed. Irregular islands of detached bone are found in the interspaces. The osteophytes lie as irregular plaques of bone in the tissues. These are partly formed from pieces of fragmented bone and partly from the cortex of the contiguous joint structures. There is an increase in the lime content of the bone near the joint.

Turney [1] stated that the disease of the ankle joint tends to assume the hypertrophic rather than the atrophic form. The tibia and fibula including the malleoli become quickly overlaid with periosteal deposits. This is the osteoplastic periostitis described by Targett,[42] and the parosteal bone mentioned by Potts.[43] Targett [42] stated that the cavity of the normal articulation of the ankle joint commonly extends at the expense of its smaller neighbors until most of the tarsal joints may be

42. Targett, J. H.: On the Tabetic or Trophic Foot, Tr. Path. Soc. London **48**:288, 1897.

43. Potts, W. J.: Pathology of Charcot Joints, Ann. Surg. **86**:596 (Oct.) 1927.

included within it. Chipault [14] described a cavity in the middle of the ankle joint resulting from a disintegration of the astragalus and the os calcis. Barker [39] said that the hypertrophic changes are more common in the ankle and that there is usually an enlargement of the tibia and fibula. Henderson [27] also mentioned the fact that the changes in the ankle are almost always associated with general enlargement of the lower ends of the tibia and fibula. He added that a fracture of the os calcis or astragalus often occurred associated with a high degree of disorganization of the joint. A marked osteophytic production, however, was not common. Rotter [44] reported a case in which within three weeks of the onset of the swelling in the ankle, the joint was so disorganized from persistent use that the external malleolus touched the ground. Turney [1] believed that the hyperplastic element in these nervous arthropathies may be regarded of primarily local origin and that it is a reaction to chronic trauma. It finds its analogue in the various forms of chronic arthritis, expressing a reaction to the irritative processes initiated within the joint.

Turney [1] thought that the seat of the disease in trophic conditions of joints was in the bone, and that any change in the cartilage was subsidiary. The mere presence of the atrophy of the bone is not characteristic, for roentgenograms have proved that it occurs in every case of prolonged or severe articular inflammation. The early appearance and the degree of this atrophy are the important factors in the neuropathic joints. The true explanation of this initial trophic change in the bone is not sensory paralysis but sensory irritation. There is ample reason clinically in regarding the osseous change underlying the group of nervous arthropathies as connected with the irritation of nerves or nervous centers. The nature of this atrophy was shown by Raymond and Onanoff [45] to be a reaction in the nature of a reflex. They set up suppurative inflammation in two corresponding joints of a rabbit, having previously divided the posterior roots on one side only. Muscular atrophy appeared as usual on the intact side, but remained absent on the side on which the posterior roots had been divided. The experiment was repeated by Hoffa [46] with the same result. Roentgenograms have shown that a reflex atrophy of bone in these circumstances is induced at the same time and in the same way as the reflex atrophy of muscle. It consists of a rarefaction of both the cancellous and the compact bony tissues, and extends far beyond the actual vicinity of the joint. There is special significance in the fact that this change in the bones is also found apart from any joint lesion in cases of injury to peripheral

44. Rotter, Josef: Die Arthropathien bei Tabiden, Arch. f. klin. Chir. **36**:1, 1887.

45. Raymond and Onanoff, quoted from Turney.

46. Hoffa, quoted from Turney.

nerves, which are of partial nature and associated with persistent irritation. It is fairly certain that a division of the nerve per se does not produce changes in bone, except so far as it causes paralysis. The effective cause is the partial division of the nerve, resulting in prolonged irritation.

Tinel [47] and Turney [1] agreed that all trophic and vasomotor disturbances are more frequent and severe in neuritic irritations than in simple division of nerves. Goodhart [3] believed that the vascular changes produced by an irritative nerve lesion are the real cause of the so-called "trophic disturbances," and that prompt relief from the irritation becomes an imperative measure to prevent complications. Campbell [21] stated that an incomplete nerve section is most likely to produce these changes in the bone, and that experiments have shown a rarefaction of bone after section of the nerves. He considered that the rarefaction occurring secondarily to nerve injuries is partly trophic in origin, the result of the disturbed vasomotor activity.

Henderson [27] said that observations on the nerves point to lesions of the terminal sensory nerves only. Pitres [48] and others, who worked particularly with the nerves to the joints, have shown a degeneration of the nerve fibers; however, there also have been demonstrated some regeneration and an increase in the nuclei in the bundles.

Eloesser's [49] experiments on cats showed that an arthropathy of this type could be produced in a traumatized joint which had been desensitized. He severed the posterior sensory roots of the cord which supplied the extremities. Tabetic fractures and arthropathies were produced in healthy animals. In the joints of three animals, whose limbs had previously been rendered anesthetic by a section of the posterior roots, following operative trauma there rapidly developed Charcot lesions. These observations are in accord with the statement of Philips and Rosenheck [50] that any joint deprived of its sensory mechanism and subject to trauma may become a typical Charcot joint.

Turney [1] found that experimental sections of nerves in animals have given the most contradictory results. Even when changes in the bones have been found, the conditions have been complicated so much by open sores or by paralysis, or by both, that no conclusions can safely be drawn. Eloesser [49] noted in his animals that many of the joints were infected, especially the ankle; he considered that these resulted from tabetic ulcers developing on the feet.

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47. Tinel, quoted from Goodhart (footnote 3).

48. Pitres, A., and Carrierre, G.: Arch. klin. de Bordeaux **5**:483, 1896; Rev. neurol. **4**:748, 1896.

49. Eloesser, L.: On the Nature of Neuropathic Affections of Joints, Ann. Surg. **66**:201 (Aug.) 1917.

50. Philips and Rosenheck (footnote 26, first reference).

The following case report of a neuropathic arthropathy of the ankle joint is presented because of the unusual opportunity to correlate the clinical, roentgenologic and pathologic observations, and because the evidence appears to be conclusive that the condition is due to a lesion of a peripheral nerve trunk.

REPORT OF CASE

History.—J. R. H., a white man, married, aged 29, was first seen on March 24, 1928, complaining of weakness and deformity of the left foot and ankle. He stated that on April 2, 1926, two years prior to this time, while working as a brakeman between two freight cars, his left foot became caught between the guard rail and the railroad track. Before he could free his foot, the train moved about 2 feet. The flange of one car wheel crushed the lower part of the left leg, causing three long, gaping lacerations, from the ankle to the knee. No bones were broken. Following the accident there was a severe infection of the soft tissues of the leg which required drainage tubes for four weeks. It took seven months for the wounds to heal completely. At this time, the patient first bore weight on the foot with the aid of crutches. Shortly afterward he returned to his work as a brakeman, with the foot tightly bandaged. He was able to work intermittently for only a month. The foot and leg were markedly swollen. Walking was accompanied with a great deal of pain and an increase in the swelling. The pain, which was most severe on sitting down after walking, was throbbing and would occasionally radiate from the ankle to the knee. The ankle seemed unusually weak. Nine months after the injury, he began to notice a grating in the ankle with a tendency for the foot to turn outward. This had steadily become worse. One year after the accident, he had the feeling on walking that the foot had come out of the socket. Occasionally there was the sensation of the extremity going to sleep. There was slight pain in the hip and knee at times. The pain, touch and temperature sensations were normal except for a slight inability at times to feel cold as well as in the right foot.

The general health of the patient was excellent. He had typhoid fever at the age of 12 and influenza at 18. There had been no operations or previous accidents. There had been occasional attacks of tonsillitis, but no attacks had occurred during the last two years. One tooth was extracted because of an abscess five years previous to examination. There had been infrequent colds with no cough or hemoptysis. The appetite had been good, and the bowels moved regularly. There had been occasional bilious spells. He said that he had not had venereal disease or any symptoms of it. He had been generally nervous since the accident. He had always done active work. His wife was living and well and had had no miscarriages. Two daughters and one son were living and well. His mother died of pneumonia. His father was living and well, as were three brothers and two sisters. There was no history of tuberculosis, cancer, insanity, heart or kidney disease in the family.

Examination.—Physical examination showed an extremely well nourished and developed man, who was suffering no pain at this time. He weighed 165 pounds (74.8 Kg.), and was 5 feet 9 inches in height. He was intelligent and cooperative. The skin and mucous membranes were normal. There was no general glandular enlargement. The shape of the head and the hair and scalp were normal. The hearing was excellent, and the ears presented no tophi or discharge. The pupils were equal and regular and reacted to light and in accommodation. The sclerae

and conjunctivae were normal. The ophthalmoscopic examination gave negative results. The nose showed a normal septum with no discharge. There was no tenderness over the sinuses. The teeth were in excellent condition, showing only a few fillings. There was no pyorrhea and the gums were normal. There were small, atrophic tonsils with no injection of the pharynx. The thyroid was not enlarged. The chest was well developed and symmetrical, with normal respiratory excursions. The apex beat of the heart was in the fifth interspace well within the nipple line. The rate and rhythm were normal, and there were no murmurs. The radial pulse was of good quality and synchronous with the heart beat. The blood pressure was 110 systolic and 60 diastolic. The lungs were normal on auscultation and percussion. The abdomen showed no tenderness, muscle spasm or masses. The liver and spleen were not enlarged. The external inguinal rings were normal. There was no evidence of scars on the external genitalia. The testes and epididymes were normal. The knee reflex was slightly exaggerated on the right and normal on the left. The Babinski, Oppenheim and Gordon

Fig. 1.—Photograph of the lower legs showing the tremendous amount of swelling and edema on the left. Notice the pigmented scar (*A*) marking the site of one of the original draining sinus tracts, and also the prominence of the lower end of the tibia (*B*) with the eversion deformity of the foot.

reflexes were normal, and there was no ankle clonus. The deep reflexes of the upper extremities were normal. The reflex of the jaw was normal. The cremasterics were absent. The abdominal reflexes were weak. There was no curvature of the spine and the motion was entirely normal. The upper extremities and the right lower extremity were entirely normal.

The main point of interest lay in the left lower extremity. There was marked enlargement of the foot, ankle and calf (fig. 1). There was an eversion deformity of the foot of about 45 degrees. The soft tissues about the ankle had a distinct doughy feel. The ankle joint showed a marked increase in fluid; however, there was no tenderness, no increase in local heat and no pain on manipulation. Active and passive motion of the ankle brought out a coarse grating. All movements could be actively carried out. Passive eversion from the resting position was about 20 degrees, while passive inversion was markedly increased, being about 60 degrees. Dorsiflexion and plantar flexion were normal. The foot was held in

about 20 degrees equinus. The lower end of the tibia was prominent, while the lower end of the fibula could be palpated only with difficulty. Many small loose fragments of bone could be felt about the malleoli. Sensory examination showed only a slight impairment of light touch with no well defined areas of hypesthesia. The toes and anterior portion of the foot showed no abnormality. There were three irregularly shaped, slightly pigmented scars, marking the sites of the old draining sinuses, about the anterior, lateral and medial aspects of the lower third of the leg. There was one fine scar extending from the anterior part of the lower third upward and laterally around the calf of about 25 cm. in

Fig. 2.—Roentgenogram taken four months after injury, showing a beginning absorption about the anterior portion of the tibia and the os trigonum.

length. There were a few dilated veins in the calf. The knee joint was not enlarged and was entirely normal. There was an apparent atrophy of the thigh. There were no enlarged lymph nodes in the groin. The left ankle was 12 cm. larger in circumference than the right. The left calf was 9 cm. larger than the right in the lower third and 3 cm. larger in the middle and upper thirds. The left knee was 1 cm. larger than the right, while the middle of the left thigh was 4 cm. smaller than the right. The patient walked with a marked limp on the left with the eversion deformity of the foot becoming much more marked. The weight which normally should be borne on the os calcis was taken by the end of the tibia.

The laboratory examination of the urine showed a clear amber color, an acid reaction, a specific gravity of 1.030, no albumin or sugar and microscopically an occasional epithelial cell and leukocyte. The examination of the blood showed 79 per cent hemoglobin, 4,270,000 red cells, and 5,900 white cells per cubic millimeter, of which 55 per cent were polymorphonuclears, 38 per cent large lymphocytes, 3 per cent mononuclears, 2 per cent eosinophils and 2 per cent endothelial cells. The Wassermann reaction of the blood and the Kahn tests were negative. The spinal fluid was of a clear color, came out under normal pressure, had 2 cells per cubic millimeter and gave a negative reaction to globulin and Wassermann tests.

Fig. 3.—Roentgenogram taken nineteen months after injury, showing an almost complete absorption of the body and neck of the astragalus, with a disintegration of the upper surface of the os calcis and the lower margins of the tibia and fibula, and numerous loose fragments of bone about the joint.

The joint fluid from the left ankle had a slightly reddish tinged cloudy appearance and contained 32,200 cells per cubic millimeter, of which 51 per cent were polymorphonuclears, 41 per cent lymphocytes, 2 per cent basophils and 6 per cent mesothelial cells. Both the Wassermann and the Kahn tests on this fluid were negative. Two separate cultures of this fluid showed the presence of *Staphylococcus albus,* which took three days to appear on the culture mediums on the first

occasion and four days on the second occasion. In aspirating the joint with a large sized needle there was the complete absence of pain as soon os the skin had been penetrated.

The roentgen examination of the left ankle, taken in August, 1926, four months after the injury (fig. 2), showed the calcification through the neck and anterior portion of the astragalus not to be as uniform as normal. There was a definite area of absorption in the os trigonum. There was an irregularity and beginning separation of the lower anterior tibial margin. There was a slight amount of atrophy through all the bones of the lower part of the leg and ankle. The outline

Fig. 4.—Roentgenogram taken twenty-three months after the injury, showing a more marked absorption and disintegration than in figure 3 with many more loose irregularly shaped bone fragments. There is also a proliferation of bone along the cortex of the fibula, and a separation of the astragaloscaphoid joint.

of the soft tissues showed a large amount of swelling. The roentgenogram of the left ankle, taken in November, 1927, nineteen months after the injury (fig. 3), showed a marked disintegration of the tibio-astragalar and astragalocalcanean joints. There had been a complete absorption of the body and neck of the astragalus. There had also been an absorption of the upper portion of the os calcis and the lower margins of the tibia and fibula. There was an osteosclerosis of the margins of the tibia and fibula and the upper portion of the os calcis.

There were many large and small, irregularly shaped masses of bone in the soft tissues surrounding the disintegrated areas. There was bone proliferation along the cortex of the tibia and fibula, extending for a distance of several inches up the shafts of these bones. There was also an irregularity about the posterior margin of the scaphoid and the anterior margin of the remaining portion of the head of the astragalus. The outline of the soft tissues showed a more pronounced swelling than on the previous examination. The roentgenogram of the left ankle, taken in March, 1928, twenty-three months after injury (figs. 4 and 5), showed the disintegration and changes in the joints previously noted to be more advanced.

Fig. 5.—Roentgenogram taken twenty-three months after the injury, showing the marked lateral dislocation of the ankle and foot.

There were many more unattached bone fragments about the joint. The disintegration of the astragalus and upper portion of the os calcis was greater. There was a separation of the astragaloscaphoid joint. The bone proliferation along the cortex of the fibula was more noticeable. In the anteroposterior view, there was a marked lateral dislocation of the foot and ankle. Roentgenograms of the lumbar spine, pelvis and hips, taken in March, 1928, showed the bones to be entirely normal. There was no suggestion of a spina bifida or other abnormality.

Operation.—Operation was performed on March 25, 1928. With the patient under a general anesthetic, the left foot and ankle were amputated in the middle

third of the lower part of the leg. The muscle tissues were found to be extremely boggy and edematous. There were two sinus tracts in the calf muscles: one extended down to a point just above the medial side of the ankle and there terminated in scar tissue; the other extended up into the muscles of the calf to a point about 4 inches below the inner aspect of the knee joint. These sinus tracts did not communicate with each other. They were both filled with the same slightly reddish, cloudy fluid which had previously been aspirated from the ankle. The posterior tibial nerve was demonstrated on the medial aspect of the calf and traced down to a point about 2 inches above the ankle joint, where it terminated in scar tissue. This was adjacent to the termination of the lower sinus tract. A portion of this nerve trunk and a portion of the wall of one of the sinus tracts were removed for pathologic section. The edematous muscle

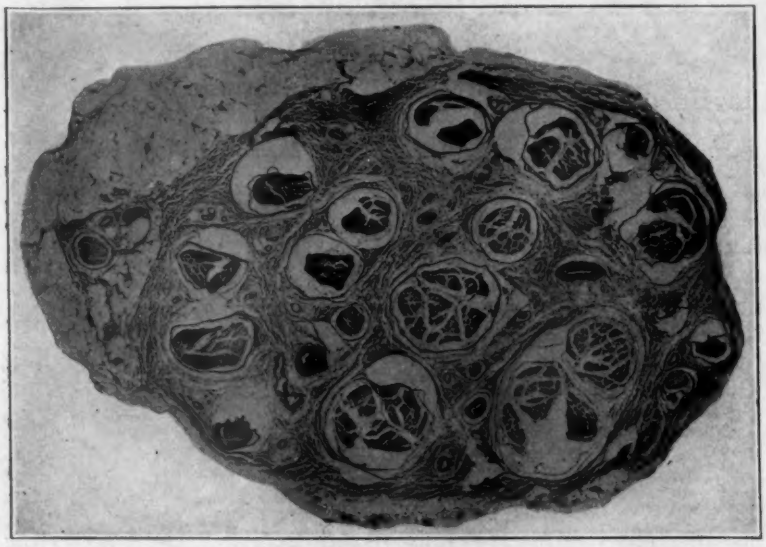

Fig. 6.—Photomicrograph of the posterior tibial nerve, showing an enormous increase in connective tissue between the nerve bundles and a generalized edema.

tissue was pulled down over the ends of the bones and sutured. The subcutaneous tissue and skin were closed without tension. One small protective drain was inserted.

After considerable drainage the incision healed in about ten weeks. There was no tendency for the incision to gape. Six months after the amputation the stump had shrunk to about one-half its previous size, and the patient was walking with an artificial limb.

Pathologic Report.—The pathologic report of the tissue removed at the time of operation was as follows: The cross-sections of the nerves showed an enormous increase in the connective tissue between the nerve bundles with a general edema in both the nerve bundles and the connective tissue (fig. 6). The cross-sections of the sinus wall showed muscle structure in which there had been a marked replacement fibrosis and myxomatous degeneration.

The pathologic report concerning the specimen was as follows (fig. 7): When the specimen was opened, there was seen a cavity between the lower end of the

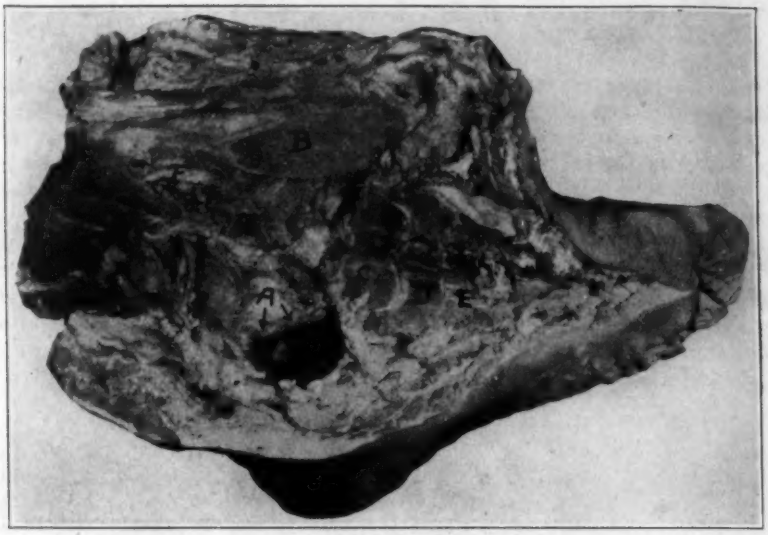

Fig. 7.—Photograph of the specimen, which has been opened. *A* indicates the cavity between the lower ends of the tibia and fibula and the bones of the tarsus; *B*, lower end of the tibia; *C*, head of the astragalus, which is the only remaining portion of this bone; *D*, scaphoid; *E*, first cuneiform, and *F*, point at which the posterior tibial nerve was found to terminate in scar tissue.

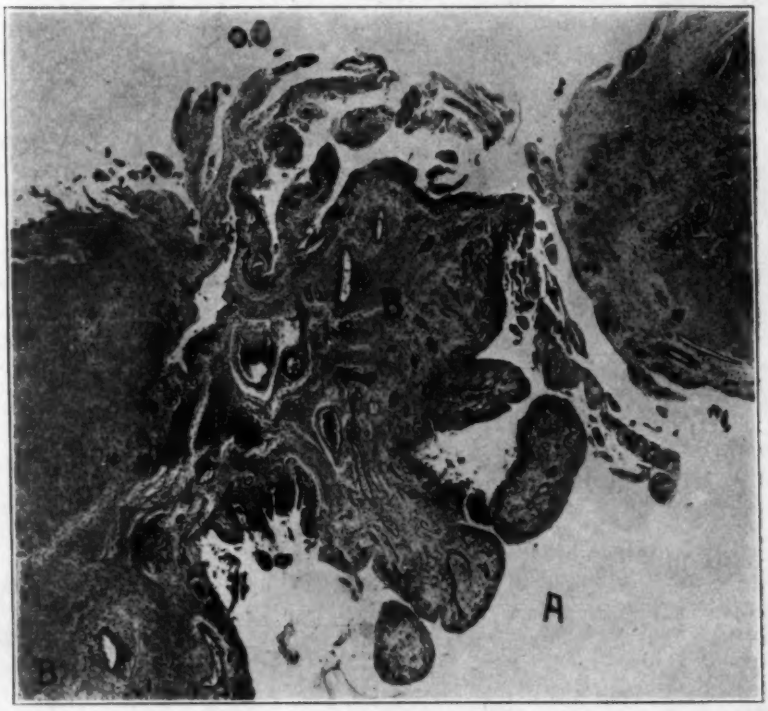

Fig. 8.—Photomicrograph (low power) showing one of the villus-like projections, which is all granulation tissue (*B*), extending into the cavity (*A*).

tibia and fibula and the bones of the tarsus, irregular in shape, roughly 8 cm. in diameter, containing a cloudy, blood-tinged fluid. Extending up the leg, apparently originating in or near this cavity, were two sinus tracts, which were rather hemorrhagic on gross examination. There were loose particles of cartilage and bone forming part of the wall of the cavity. The lining membrane was rough with villus-like projections over the various parts of the surface somewhat irregularly placed. The microscopic examination showed these villus projections to be in part cartilage and in part dense fibrous tissue, the nuclei being separated for considerable distances by strands of collagenous fibers (fig. 8). The vascular fragmentations were extremely abundant (fig. 9), forming granulation-like tissue simulating angioma, while on the actual surface there were masses of fibrin, in which were meshed some hemolyzed blood corpuscles and a few leukocytes, the

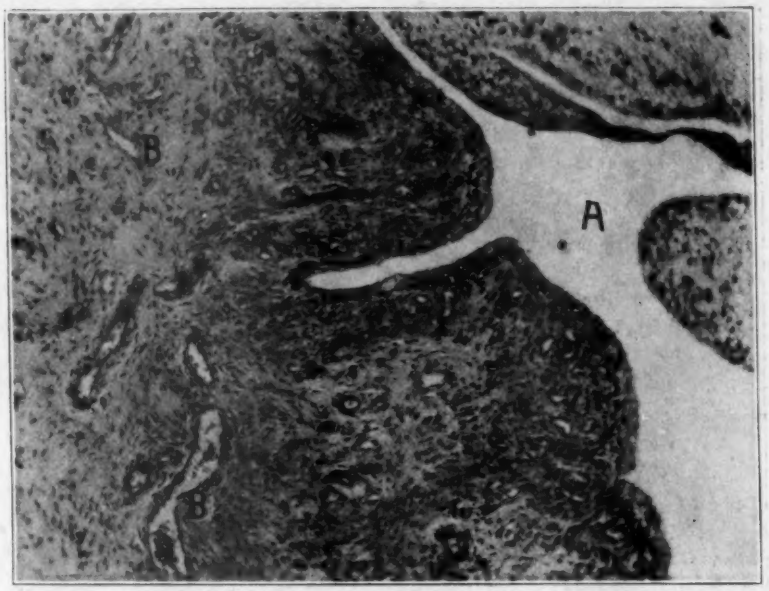

Fig. 9.—Photomicrograph (high power) showing the extremely vascular character (*B*) of the granulation tissue in the villus projection extending out into the cavity (*A*).

polymorphonuclear variety predominating. Sections through the bone showed a chronic inflammatory process characterized by replacement of the marrow by fibrinous connective tissue, there being practically no remaining marrow cells in the pieces of bone examined, which included a section from the end of the tibia and smaller masses of bone found about the cavity wall (fig. 10). Sections from the sinus in the leg showed dense fibrous tissue replacing muscle surrounding the sinus tract, which was lined by hemorrhagic granulation tissue (fig. 11). The cells of the capillaries appeared exceedingly active, suggesting an angiomatous formation. Grossly, nerves had been caught in scar tissue about these sinuses and could not be followed through. In the microscopic sections, the nerves could not be followed except for a short distance, fading away into fibrous tissue without

the formation of a definite neuroma. Traversing the fibrous tissue were occasional fibers, which presumably represented remnants of nerves (fig. 12). The inflammatory reaction was of a relatively low grade, except for the presence of hemorrhage along the sinus and the fibrinous exudate on the lining of the cavity.

COMMENT

The majority of the neuropathic arthropathies observed are those joint conditions found in tertiary syphilis spoken of as Charcot joints. This is generally described as a rapid, painless disorganization of the joint structures, due to disease of the sensory nerve tracts supplying this part. Any joint of this type with a suspected etiology of different

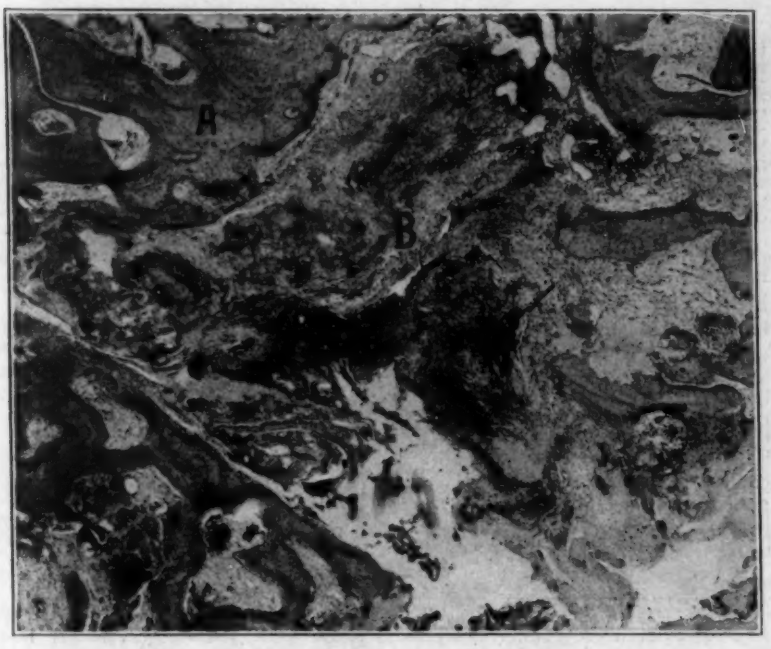

Fig. 10.—Photomicrograph (low power) showing bone from the end of the tibia. There is noted rather marked bone destruction (*A*) with an invasion of the marrow cavity with inflammatory tissue (*B*).

character should first be proved to have no association with syphilis before this cause can be accepted. In this patient there was no evidence of syphilis, as shown by (1) negative Wassermann and Kahn tests of both the blood and the joint fluids, (2) a negative Wassermann reaction of the spinal fluid, (3) the lack of any history of possible syphilitic infection and (4) the lack of any clinical manifestations of syphilis.

At the time of the amputation of the ankle, the posterior tibial nerve was traced down to a point above the medial aspect of the joint, where it terminated in scar tissue. It was impossible to determine whether

the nerve at this point had been wholly or partially severed at the time of the injury, or whether, following the infection of the soft parts of the leg, the nerve trunk also became infected and later was obliterated by scar tissue. In view of the present conception of the development of these neuropathic arthropathies, it is most likely that there was either a partial division or an infection of the nerve, which resulted in an irritative nerve lesion. The sections of the portion of this posterior

Fig. 11.—Photomicrograph (high power) showing the wall (*B*) of a sinus tract (*A*) with fibrin along margin. A marked fibrosis (*C*) can be seen surrounding the remaining muscle tissue (*D*).

tibial nerve removed at the time of the operation show a marked increase in connective tissue between the nerve bundles and a generalized edema (fig. 6). The posterior tibial nerve supplies the main articular branches to the ankle as well as to the astragalocalcanean and the astragaloscaphoid joints. With a prolonged irritation of this nerve trunk, subsequent changes in the joints supplied would be expected. It is rather interesting to note the circumscribed area adjacent to one of the sinus tracts, distal to the point at which the posterior tibial nerve ended in scar tissue,

shown in figure 12. This resembles a hyalinized nerve bundle, although no definite nerve structure can be made out. There were also in the fibrous tissue in this area occasional nerve fibers, which were thought to represent remnants of the original nerves. These anatomic evidences of disturbance of innervation of the part point toward a peripheral nerve lesion as being the primary etiologic factor of the arthropathy. There

Fig. 12.—Photomicrograph (low power) showing a cross-section of one of the sinus tracts (*A*), containing some fibrin (*C*), adjacent to which is a circumscribed, lighter stained area, which is thought to be a hyalinized nerve bundle (*B*), although no definite nerve tissue can be demonstrated.

were two significant clinical evidences of neurologic character, which showed a disturbance of the sensory mechanism. First, the pain in the ankle on weight-bearing and walking was not commensurate with the pain which would be expected to accompany this amount of joint disintegration if the sensory nerves were not involved; second, there was

complete absence of pain when the joint structures were pierced with an aspirating needle. The latter is spoken of as Eloesser's [51] sign, but was first described by Oehlecker [52] (1914).

The changes seen in the roentgenograms form an interesting part of the picture. Steindler [33] stated that the x-ray pictures demonstrate small infractions and fissures to be the first changes in these joints. The first roentgenogram of the ankle taken four months after injury shows these early changes (fig. 2). At this time, the only trauma the joint had received was that associated with the accident. No weight had been borne on the ankle since injury. Nine months after the accident the patient first started to walk, and it was shortly after this that he noticed a grating as if the ankle were out of place. This weight-bearing on a joint that previously had been almost completely desensitized through an injury to its nervous mechanism was the direct cause of most of the pathologic changes. The experimental work of Eloesser [49] tends to confirm this clinical observation. The second roentgenogram taken nineteen months after the injury shows the changes to be far advanced (fig. 3). At this time, the patient had been walking on the ankle for about one year. Four months later, the third roentgenogram presents even more marked changes, with a great many additional plaques of bone about the joint (fig. 4). The anteroposterior roentgenogram shows a marked lateral dislocation to be present (fig. 5). All of the changes in the bone described by Ridlon and Berkheiser [53] can be seen in these roentgenograms, namely, atrophy of the bone ends, osteoporosis with erosion, osteosclerosis, proliferation of irregularly shaped bone masses and osteophytes. The parosteal bone of Potts [43] or the osteoplastic periostitis of Targett [42] can be observed to extend well up the shaft of the fibula.

The development of the sinus tracts within the calf and the cavity found in the ankle joint are unusual features of the condition. The lower one of these sinus tracts in the calf apparently at one time connected with the cavity in the ankle (fig. 7). Targett [42] and Chipault [14] have both described this cavity which forms in the ankle joint with the progressive development of the arthropathy. Rotter [44] reported a case of neuropathic arthropathy in which synovia or serous fluid was removed from the submuscular tissue at some distance from the joint, but did not describe any sinus tract formation. The villus-like projections (fig. 8) found in the cavity and sinus tracts apparently were formed by the

51. Eloesser, L.: A Sign Occurring in Tabes Complicated by Charcot Joints, J. A. M. A. **77**:604 (Aug. 20) 1921.

52. Oehlecker, F.: Ein weiterer Beitrag zur Klinik Unfallbegutachtung und Behandlung tabischer Gelenkerkrankungen, Beitr. z. klin. Chir. **92**:599, 1914.

53. Ridlon, John, and Berkheiser, E. J.: Neuropathic Arthropathies, Charcots Spines, J. A. M. A. **79**:1467 (Oct. 28) 1922.

organization of the fibrin. In some of these villi, cartilage cells were found. It is likely that these became enmeshed in the fibrin after sequestration from the joint surfaces as small bits of cartilage. The nutrition in the fluids was sufficient to keep these cartilage cells alive, so that they proliferated to form the small nodules found in the walls of the sinuses and cavity. The lower end of the tibia was found to be covered with cartilage-like tissue, which probably represents an attempted repair of the normal hyaline cartilage. The invasion of the bone-marrow of the lower end of the tibia with fibrous and granulation tissues is what would be expected with these pathologic conditions (fig. 10).

The extensive fibrosis and edema found in the muscle tissue taken from the calf (fig. 11) is in keeping with the gross changes in this part. Through this muscle tissue, as well as through the walls of the sinus tracts, there was a rather extensive vascular proliferation (fig. 9). The two cultures of *Staphylococcus albus* from the joint fluid of the ankle are indicative of an infection. These are not believed to be a contamination because of the slow appearance time on the mediums. The extremely high cell count with a predominance of polymorphonuclears in this fluid also favors the presence of an infection. It is interesting to note the extremely high percentage of mesothelial cells in this fluid, which cells are characteristic in the joint fluid in low grade arthritic infections. This infection is undoubtedly responsible for a great many of the changes through the muscles and tissue in the calf and ankle.

There have been reported instances of neuropathic joints associated with a spina bifida and injuries to the spinal column. This possibility in the patient is ruled out by negative roentgenograms of the lumbar spine and pelvis and a negative history of injury to the lower part of the back.

CONCLUSIONS

1. A classification of the neuropathic lesions of the bones and joints is presented.

2. A case of neuropathic arthropathy of the ankle is reported.

3. The etiologic factor in this case appears to be a peripheral nerve lesion, as the posterior tibial nerve was found to terminate in scar tissue above the joint.

GENITAL PROLAPSE FOLLOWING TOTAL HYSTERECTOMY

A SUCCESSFUL OPERATIVE PROCEDURE *

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Total removal of the uterus is a definitely indicated surgical procedure for several gynecologic conditions. Vaginal hysterectomy is a development which has followed the necessity of total removal of the uterus. This procedure has become very popular in the average operating room, as the technic is easier than that of the abdominal operation and the mortality rate is much lower. By the abdominal route the problem of supporting the bladder and vault of the vagina is much more readily handled than by the vaginal route.

In the early nineties, Pryor popularized vaginal hysterectomy through the use of his clamps. Since that period a much better operation for the removal of the uterus by the vaginal route was offered by Dr. Charles Mayo and has been adopted more or less universally. In the Pryor operation there was no provision made against the possibility of prolapse of the vagina and bladder other than the perineal supports. In the Mayo operation, the broad ligaments are brought together and the bladder so fixed that vesical and vaginal prolapse is skilfully prevented in the majority of these operations.

However, after any type of vaginal hysterectomy a marked genital prolapse often happens in which the vagina becomes completely everted and the bladder partially or completely protrudes. With the cervix and its attached supports entirely wanting in these cases, the problem of returning the bladder to the abdomen and fixing it there through any type of vaginal operation, is, practically speaking, impossible.

In all the literature and textbooks on this question of genital prolapse after total removal of the uterus the only procedure offered to relieve this trouble is colpocleisis. Simon, in 1885, originally recommended and described colpocleisis for the cure of intractable vesicovaginal fistula, but for the past twenty-five years or more, colpocleisis has been undertaken repeatedly for the cure of genital prolapse after total removal of the uterus. Needless to say, not only is this operation a poor surgical procedure, which is rather difficult to accomplish properly and gives a poor result in many instances, but it is definitely deforming.

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* Presented at the Annual Meeting of the Medical Society of Virginia, Charlottesville, Va., Oct. 23, 1929.

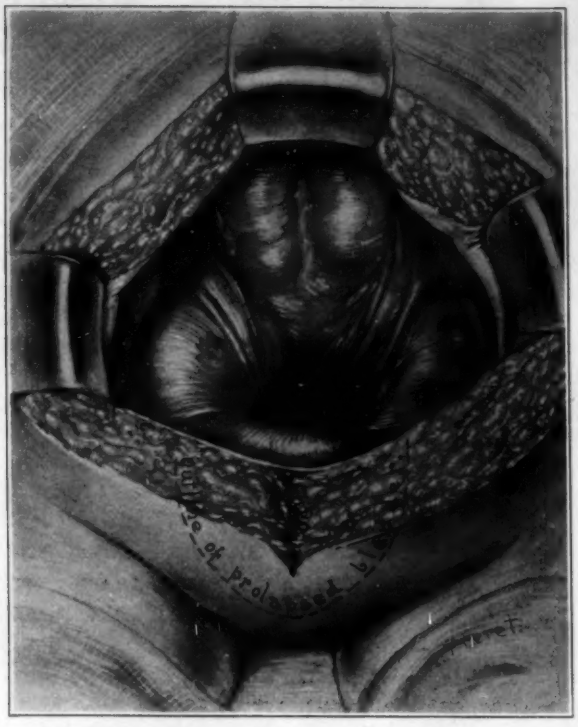

Fig. 1.—A diagrammatic sketch showing the funnel-shaped appearance of the pelvis when the abdomen is opened and before the bladder and vaginal prolapse have been reduced. It will be noted that the two broad ligaments, consisting of the round and infundibulopelvic ligaments, together with the fibrous structures between, are drawn down and attached to the apex of the funnel the smaller end of which coincides with the upper end of the vagina where the cervix was originally located.

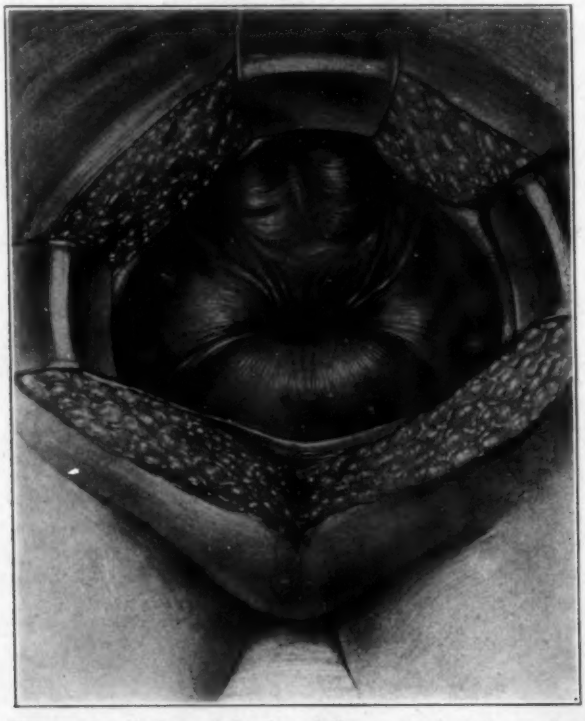

Fig. 2.—The same relation of the broad ligaments, but the vagina and bladder have been returned to the normal position.

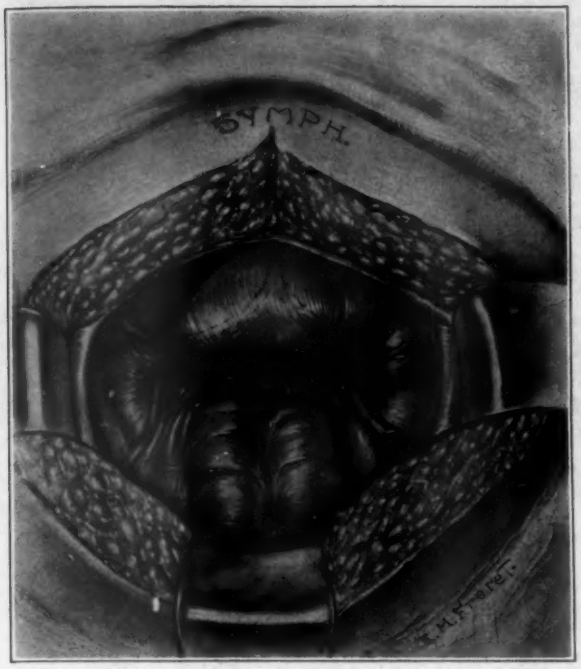

Fig. 3.—The same relationship of the pelvic structures, with the patient in the Trendelenburg position. It will be noted that the bladder is rolled upward and completely covers the apical attachments of the broad ligaments to the upper end of the vagina.

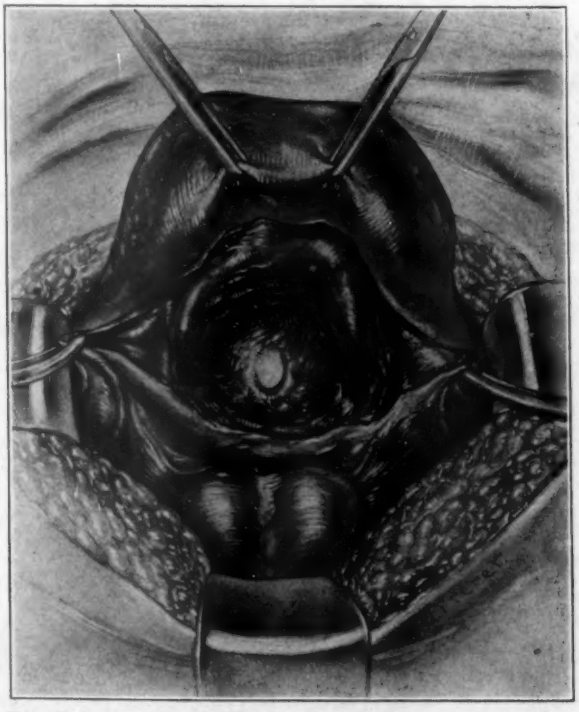

Fig. 4.—The first step is the introduction of the Cameron light through the vulva to the upper end of the vagina. This acts as a mechanical guide; the glow of the light readily facilitates the identification of structures. The dissection provides for the complete freeing of the bladder anteriorly, the broad ligaments laterally and the rectum posteriorly from the vagina. In the average case the vagina will then represent a raw cone from 1½ to 2½ inches (3.8 to 6.3 cm.) long.

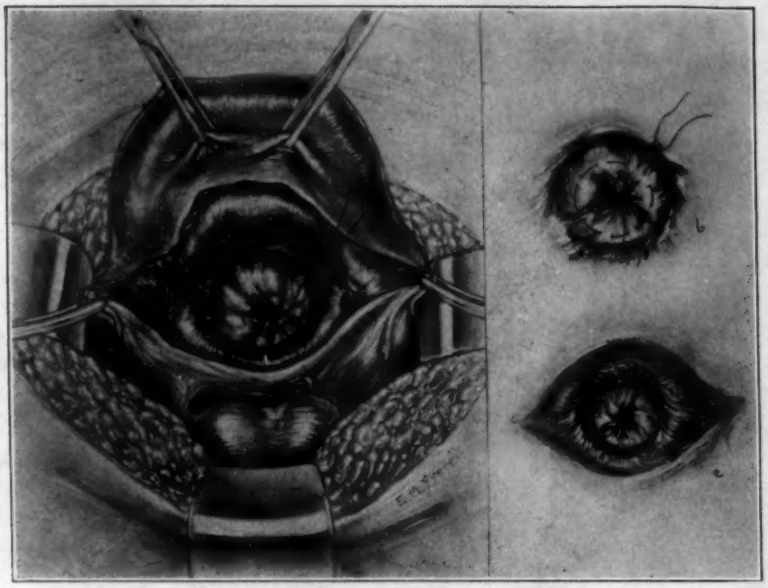

Fig. 5.—With the pelvic portion of the vagina completely freed on all sides, the next step consists of the introduction of three purse-string sutures of silk, *a*, *b* and *c*. Each purse string is tied before the next one is put in; this results in an infolding mass of the upper end of the vagina which provides a kind of plug for the outlet and at the same time shortens the normal depth of the vagina, depending on its individual length. The average reduction in length is about half.

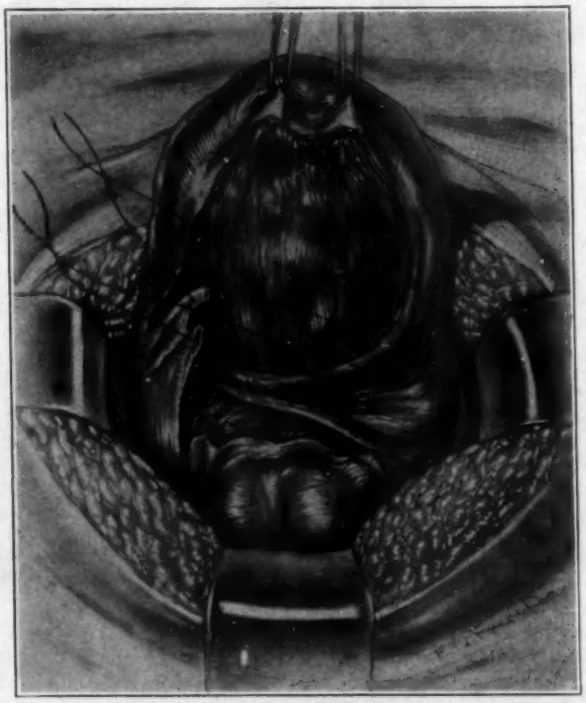

Fig. 6.—After the infolding of the vagina, the broad ligaments are brought obliquely across the vaginal ball and sutured snugly to fibrous structures on each side of the vaginal stump.

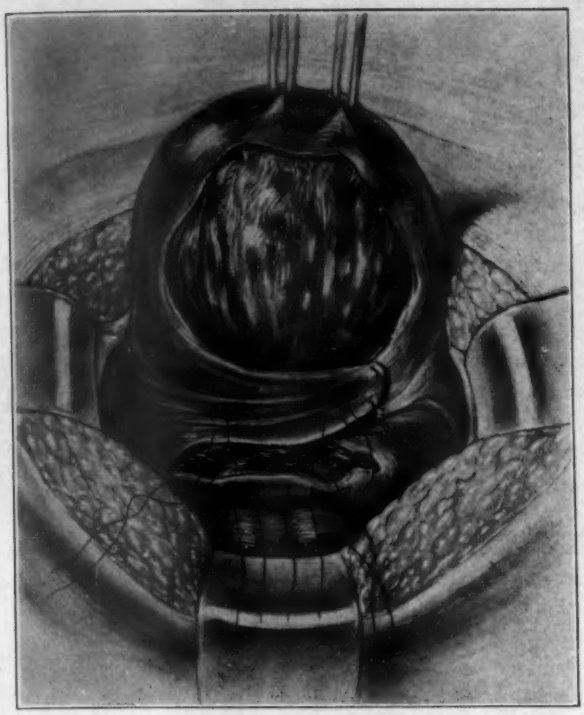

Fig. 7.—Both broad ligaments are overlapped and snugly sutured behind the bladder and as near to the apex or trigone as is possible, thus providing an additional sling or hammock on which the bladder can be supported.

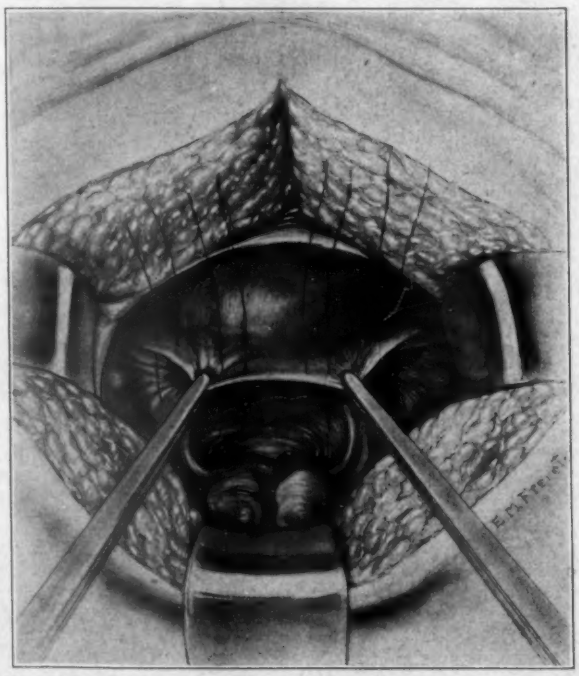

Fig. 8.—The final step, in which the bladder is brought backward over the constructed supports and sutured to the posterior pelvic area in a manner that will cover up all raw surfaces. Following the closure of the abdomen, a snug, high perineal repair is always done according to the technic previously described (Payne: A Technic for the Repair of Relaxed or Lacerated Perineum, J. A. M. A. **78**:574 [Feb. 25] 1922).

This problem of genital prolapse presented itself to me about fifteen years ago. After obtaining no help from my confrères or from the literature, I finally devised the technic given in the accompanying illustrations and legends. I have done this operation only four times, the last one two years ago and the first one more than ten years ago. In these four cases, the result has been entirely satisfactory. I am describing it here with the hope that it may be of some help to other operators and, through a greater trial of the procedure, thus to determine its value from the standpoint of a temporary or a permanent cure.

This is not claimed to be a new operation; all the steps or principles have been utilized for years in other gynecologic problems. The technic merely covers the application of well known principles which, as far as I can discover, have not been described in the literature or applied to the handling of this particular problem of prolapse after total hysterectomy.

CHRONIC IDIOPATHIC DUODENAL ILEUS ASSOCIATED WITH HYPERTHYROIDISM

REPORT OF CASES, ONE WITH ANATOMIC OBSERVATIONS *

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Chronic duodenal ileus or obstruction may be divided into several types. It may be idiopathic, or it may result from some abnormality or pathologic condition, including postoperative complications. Idiopathic ileus may be (1) adynamic or paralytic; (2) dynamic, due to excessive muscle contraction, or (3) mechanical.

Clinically, the course may be persistent, intermittent or remittent.

The location of the obstruction may be in any portion of the duodenum. In this study, however, the nonparalytic type of idiopathic ileus is chiefly considered, with the obstruction at the terminal duodenum.

Numerous theories and predisposing factors have been advanced for this condition, with little supporting evidence. However, no reference has been noted in the literature to the association with hyperthyroidism.

The anatomic postmortem observations in one case add unusual interest.

REPORT OF CASES

CASE 1.—*History.*—J. W., a man, aged 39, married, entered the Presbyterian Hospital on March 12, 1926, and was discharged on Sept. 16, 1926. The chief complaints were palpitation of the heart, tachycardia, nervousness and extreme weakness. The patient had two children who were living and well. He was employed in an office and had had considerable business worries during the last few years. He smoked a great deal.

The onset of symptoms began about two weeks previously with tachycardia, which persisted, with attacks of palpitation.

During the first week, he stated that he had an aching and soreness over his body as though he were having grip. During the second week, he was restless at night and had little sleep. He had noticed an enlargement of the neck during the last few days. Weakness had been marked at times and had been accompanied by a feeling that he might collapse. He had lost some weight during the last ten days. His normal weight recently had been about 180 pounds (81.6 Kg.). There had been a tremor of the hands noticeable during the last few days. The appetite had been good.

Many years previous to admission, the patient had two attacks of pneumonia. Rheumatic pains were present for a short time several months before admission

* Submitted for publication, Oct. 25, 1929.

to the hospital, after which he had a short vacation, and felt well. He had influenza twice several years prior to the present illness and occasionally had sore throat.

Four years previous to the present admission, he entered this hospital during a subacute attack of appendicitis. In his history, he stated that a few months previously he had experienced two attacks of unusually severe distress following the eating of pork, which nearly always occasioned some distress. This was associated with belching of gas, which lasted one night. There was no other history of stomach or gallbladder trouble. An Ewald test meal was given and showed a free acid of 35 and a total acid of 70. A seven hour motor meal contained about 3 ounces of solids which contained free acid. At that time, I removed a subacutely inflamed appendix and a gallbladder filled with faceted stones. The surface of the liver was gray and thickened. A piece removed at the time showed chronic hepatitis microscopically. There have been no subsequent symptoms of stomach trouble.

Physical Examination.—The patient was about 6 feet tall and was thin. He was extremely nervous. Exophthalmos was slight, but other eye symptoms of exophthalmic goiter were moderately advanced. The tonsils were hypertrophic and cryptic. Roentgenograms of one tooth showed some evidence of apical infection.

There was a diffuse moderate enlargement of the thyroid gland, including the isthmus. There was a bruit and pulsation over the gland.

The pulse rate was rapid. Auricular fibrillation was present at times.

The abdomen was slightly retracted and tense. The old operative scar was firm.

The extremities were constantly in motion. There was a marked coarse tremor of the fingers. The reflexes were normal.

Results of the examination were otherwise negative.

The course of the hyperthyroidism was unusually severe (fig. 1). The heart was dilated, and auricular fibrillation was frequently present. The nervous symptoms were marked. His condition was so serious after four weeks of treatment with a compound solution of iodine that the superior thyroid arteries were ligated at an interval of one week. Almost immediately he became delirious, and the administration of the solution had to be stopped because it aggravated his symptoms. The delirium, which was maniacal at times, continued for about two months. Emaciation became marked, and at times the patient was in a dying condition. He lost more than 90 pounds (40.8 Kg.) within a few weeks. Attacks of acute cardiac decompensation with cyanosis occurred. Dextrose was given intravenously a number of times, and a digitalis preparation was given regularly. Morphine had to be given continuously in doses of 2 grains (0.13 Gm.) a day but did not control the delirium. The large doses had to be kept up for several weeks after the delirium.

Vomiting occurred at intervals during the delirium. Near the close of it, at one time there was a large amount of sugar in the urine with a trace of diacetic acid.

Hunger was marked for about ten days following the delirium, when the patient was given double portions of food. The intake of fluid averaged 4,000 cc. a day.

During this time, cramps were first complained of with some distention in the upper part of the abdomen, and peristaltic waves were noticed. For a period of ten days, there were diarrhea and persistent vomiting. On July 2, a roentgen-

ologic examination proved the condition to be a marked duodenal obstruction. Medical management, with small, frequent feedings and changes of position, including elevation of the pelvis, was instituted. An attempt was made to pass a duodenal tube, but the patient refused.

For about a month, there was no vomiting, but the colicky pains and visible duodenal dilatation persisted after the intake of all fluids. During this period, acute decompensation of the heart recurred for a few days, with edema over the dependent portions of the body and an enlarged liver. This condition improved, but two days after again starting the administration of compound solution of iodine there were diarrhea and vomiting of 1,200 cc., which occurred every other day for six days. The dilated duodenum was visibly larger, and the peristalsis was more marked, passing chiefly from right to left. At the end of eight days, the patient had lost 19 pounds (8.6 Kg.), but his heart and hyperthyroidism

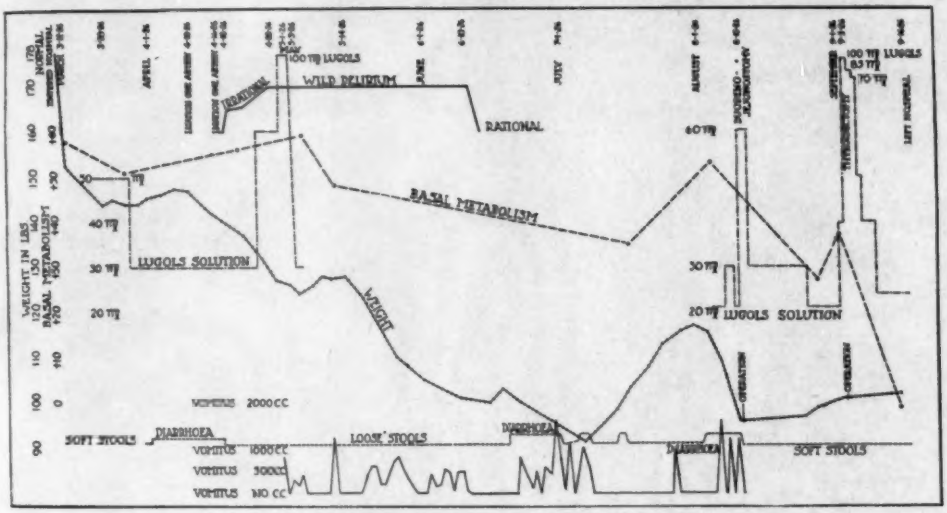

Fig. 1 (case 1).—The clinical course of chronic idiopathic duodenal ileus, developing during acute hyperthyroidism.

seemed improved. A similar temporary clinical improvement, especially of the condition of the heart, was noted previously on a number of occasions which were associated with loss of weight and dehydration.

At this time, the patient was in a desperate condition from the duodenal obstruction, and a duodenojejunostomy was decided on.

Laboratory Examination.—The basal metabolism rate was plus 57 at the time of entrance. It remained high until after the duodenojejunostomy, when there was a slight fall with a subsequent rise. After thyroidectomy three weeks later, it dropped to normal.

The urine showed a trace of sugar at the time of admission. During the delirium, there were, intermittently, a trace of albumin and a few casts. At one time, near the end of delirium, June 6, there was a large amount of sugar with some diacetic acid. During the last month, when dilatation of the duodenum was visible daily, the urine was normal with the exception of an occasional trace of albumin with a few casts.

The Wassermann reaction of the blood was negative.

When the patient was admitted to the hospital, the hemoglobin was 98 per cent and the white blood count was 7,400. The blood pressure was 124 systolic and 76 diastolic. After two months of delirium with a loss of one-half the body weight there was a little drop in the hemoglobin and number of red blood cells. On May 6, a test showed no hemolysis or agglutination of erythrocytes in various dilutions of a physiologic solution of sodium chloride with a 6 per cent dextrose solution. The blood calcium on June 7, late in the delirium, was 13.55 mg. On June 7, while the patient was delirious and critically ill, the carbon dioxide volume was 51.3 per cent and the blood sugar was 106.6 mg. per hundred cubic centimeters. On June 28, during the symptoms of marked dilatation of the duodenum, the carbon dioxide volume was 56 per cent.

On July 2, during the time of almost complete obstruction of the duodenum, as shown by the x-rays, the urea nitrogen was found to be 36.68 and the blood chlorides 445 mg.

The stools were yellow or brown and were usually soft and mushy, but watery at times. Occult blood was usually absent.

Roentgenologic Examination.—On July 2, after ten days of severe obstructive symptoms (fig. 2), the patient was weak and could not stand. He did not take a full mug of barium sulphate. There was considerable fluid in the stomach, which was large and dilated. Peristalsis was rather slow during the time of observation. Definite peristaltic waves were seen closing off the end of the antrum. By turning the patient a little on one side, the barium passed through the pylorus and filled the duodenum, which was distended from three to four times the normal size. There seemed to be a good cap. After several minutes, and on turning the patient to the left side, a trace of barium was seen in the small bowel beyond the duodenum. The patient was so weak that further observations could not be made. The roentgenograms at this time showed a large dilated stomach, a patent dilated pylorus, a fair duodenal cap and extremely large dilated second and third portions of the duodenum. The point of obstruction as determined from the fluoroscopic examination and the roentgenograms was apparently near the duodenojejunal flexure, but owing to the lack of filling of the terminal duodenum over the vertebra, the actual point of obstruction could not be determined. The pylorus was situated over the third lumbar vertebra, and the duodenojejunal flexure was somewhat to its left.

Duodenojejunostomy.—On Aug. 10, 1926, with the patient under ethylene anesthesia, a duodenojejunostomy was done. The abdomen was opened to the right of the midline. The transverse colon was lifted up, and the duodenojejunal flexure appeared to lie near the vertebra. The jejunum, which was of normal size, turned and extended downward directly into the pelvis. The remainder of the small intestine was entirely in the true pelvis. A loop of jejunum was brought up to the transverse infracolic portion of the duodenum, where a lateral anastomosis was made. Silk was used for the outer layer and catgut for the inner layer of sutures. No clamps were used. Considerable retroperitoneal fat was present in spite of the marked emaciation. The duodenum was empty and did not appear to be greatly enlarged. Several stitches were taken at each end of the union to prevent angulation of the jejunum.

Following the duodenojejunostomy the obstructive symptoms were permanently relieved, and food was taken without further distress. No more peristaltic waves were seen. Compound solution of iodine was given. A subtotal thyroidectomy was done twenty-four days later.

Thyroidectomy.—On Sept. 3, 1926, with the patient under ethylene anesthesia, a subtotal resection of both lobes of a large thyroid and isthmus was done. The parathyroids were unusually plainly visible and were avoided. A crisis was passed at the thirtieth hour with a temperature of 104.4 F. Convalescence was then uneventful.

Pathologic Changes of the Thyroid Gland: The specimen consisted of two large portions which weighed 140 Gm. They were moderately firm and had

Fig. 2.—Roentgenogram of the markedly dilated duodenum and stomach, in the horizontal position, after ten days of acute obstructive symptoms.

several nodules of increased consistency. There were several encapsulated, round, cystlike areas filled with gray, glistening mucoid material. The largest of these was 1 cm. in diameter. The stroma was gray and rather fibrous. The microscopic examination showed hyperplasia and hypertrophy.

Course.—Two months after operation, the patient had gained 80 pounds (36.3 Kg.) in weight, and there were no complaints. At this time, a fluoroscopic

examination was made and roentgenograms were taken. There was no evident dilatation of either the stomach or the duodenum, which emptied barium readily through the duodenojejunostomy stoma. When the patient was lying down, some of the barium passed out normally through the terminal duodenum, which was nearly horizontal (fig. 3). The third and fourth portions of the duodenum had considerable mobility to the left. When the patient was standing, the terminal duodenum appeared almost vertical with the formation of an acute angle in the jejunum, which may have been the result of the duodenojejunal anastomosis. The terminal duodenum was at the level of the upper edge of the fourth lumbar vertebra. The pylorus was about the same level, but appeared slightly higher in the recumbent position.

Fig. 3.—Roentgenogram taken two months after duodenojejunostomy, in the horizontal position. Complete relief from symptoms. The normal appearing duodenum emptied partly through the newly formed stoma and partly through the terminal segment with no evidence of obstruction.

About four months after operation, the patient suffered a severe mental shock from a business reverse and was acutely depressed. He developed auricular fibrillation and tachycardia for several days. One month later, he started a new kind of work, apparently feeling physically well. Two weeks later, he was found dead from drowning.

Postmortem Report.—The anatomic diagnosis was: marked vesicular emphysema (asphyxiation from drowning); hyperplastic and hypertrophic parenchymatous thyroid, both lobes partially removed; persistent lymphoid tissue of the thymus; slight chronic fibrous myocarditis; chronic diffuse nephritis; secondarily

contracted kidneys; moderate hyperplasia of the spleen; fatty changes of the aortic lining; fibrous adhesions between the anterior abdominal wall and the great omentum; lateral anastomosis between the duodenum and the jejunum; long since absent gallbladder and appendix vermiformis; and right fibrous pleuritis.

The body measured 185.5 cm. in length. A loop of jejunum crossed the front of the spine horizontally just behind the transverse colon. The weight (estimated) of the liver was 1,500 Gm., and the edges were sharp. The borders of the spleen were sharp; it measured 12 by 15 by 8 cm.

The weight (estimated) of the kidneys was 300 Gm. They had a free capsule, and the surface was slightly uneven, suggestive of a "granular" kidney. On section, the cortex of the left kidney was from 4 to 6 mm., the right, from 6 to 7 mm. The cortical markings were fairly well defined. The medulla was light purple and definitely opaque. The pelvic fat was plentiful and the pelvic mucosa unaltered.

The thyroid consisted of a zone from 1.5 to 1.8 wide on the right side and 1.6 on the left. It was grayish brown and the colloid was clearly visible. Attached on the left side lower down, there was an additional encapsulated mass of thyroid 2.5 cm. in diameter, translucent and gelatinous.

The stomach contained 60 cc. of watery fluid. The pyloric ring was 3.3 cm. in circumference.

The heart was 16 by 12 by 8.5 cm. and weighed (estimated) 450 Gm. The right side was convex. The myocardium was opaque and brownish gray. The width of the left ventricular wall was 1.5 cm. and that of the right, from 1 to 3 mm. The mitral orifice was approximately 13 cm. in circumference, the aortic 9.7, the pulmonary 9.7 and the tricuspid 15 cm. The depth of the left ventricle was 11.5 cm. The left coronary artery was 1 cm. in circumference, the left descending 0.7 and the right 0.7 cm.

Microscopic Examination: Sections of the thymus contained an abundance of lymphoid tissue and many Hassel's corpuscles. Only at the periphery of the section was there slight replacement of the lymphoid tissue by fat.

In sections of the thyroid, there were fields of connective tissue with scattered acini, near the periphery of the gland; elsewhere the tissue was practically all glandular, being made up of small and large acini containing a uniformly stained pale and purple material. The epithelium was in places cuboidal, elsewhere columnar and the latter formed papillae-like infoldings into the lumen of the acini. In the fields of columnar epithelium there were collections of round cells.

In the myocardium there was some connective tissue increase in the intermuscular spaces. A few of the small capillaries were filled with polymorphonuclear leukocytes and red blood cells and some had a perivascular round cell infiltration. The muscle fibers were extensively fragmented. The liver had some thickening of its capsule by connective tissue, which was infiltrated with round cells. There was a rather marked infiltration of round cells in the portal spaces. Changes in the parenchymal cells were negligible.

The capsule of the kidney was thickened, and in the cortex were many collections of round cells and strands of connective tissue traversing the entire cortex. The epithelium was swollen and the cytoplasm granular. The glomerular tufts were engorged with blood and the capsule unchanged.

The evidence pointed to the fact that death was due to drowning. To what extent natural causes contributed could only be speculated. The heart, thyroid and kidneys, however, all showed morbid changes, and those in the heart were sufficient to cause heart failure under sudden exertion.

The anatomic studies of the specimen of duodenum and related structures were made (fig. 4) by me. The duodenum was empty and corresponded to the circular type with no definite angles, but the horizontal, descending, transverse and ascending portions could be identified. The wall was apparently of normal thickness.

The circumference of the duodenum was 4.5 cm. in the first portion, while the second portion was slightly enlarged and measured 8 cm. at the level of the ampulla of Vater, and 7 cm. proximal to the duodenojejunostomy stoma which measured 1.5 cm. long by 1 cm. wide. At one end there was a silk suture but no evidence of ulcer.

The root of the mesentery broadened out in a triangular shape to measure 4 cm. broad at its crossing over the duodenum, with the artery and vein lying near

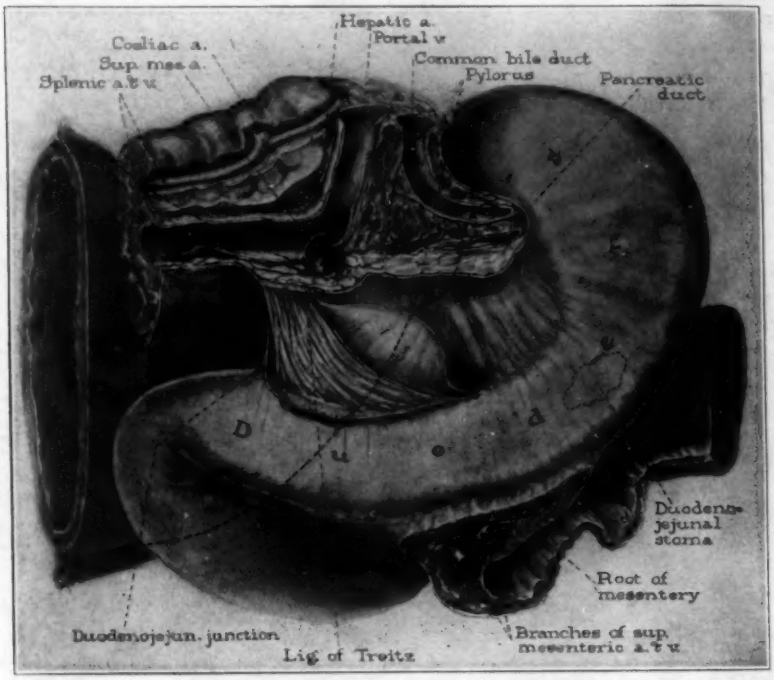

Fig. 4.—Drawing of the duodenum and adjacent viscera, removed at necropsy, viewed posteriorly. A slight dilatation of the descending portion and none of the remainder of the duodenum could be demonstrated. There was a slight definite narrowing of the duodenum beneath the blood vessels in the mesentery, but none at the duodenojejunal flexure.

the middle. The circumference of the duodenum for about 2 cm. beneath the root of the mesentery was narrowed down to 4.8 cm., while proximally it was 6.5 cm., and distally, 5.2 cm. Here, the duodenal mucosa was flattened out and adherent, while it was redundant, both proximally and distally. The narrowed segment beneath the mesentery was apparently the site of the former obstruction.

The terminal end of the duodenum beyond the mesentery measured 6 cm. in circumference, with no evidence of kinking. The jejunum was larger and measured 7.8 cm. in circumference below the stoma.

The distance from the pylorus to the ampulla of Vater measured 12 cm., to the duodenojejunum anastomosis 20 cm., to the right side of the root of the mesentery of the small intestine 24 cm., to the crossing of the superior mesenteric artery 27 cm. and to the duodenojejunal juncture 31 cm.

The muscle fibers of the ligament of Treitz passed as a band 1.5 cm. wide slightly to the left of the superior mesentery artery and directly downward on its left side to insert on the duodenum. They inserted 5.5 cm. along the duodenum, extending 1.5 cm. to the right of the superior mesenteric artery. By gentle traction on the artery I could produce a constriction of the duodenum beneath it. Beneath the artery separating it from the duodenum there was only a 2 mm. layer of fat, while it was 5 mm. thick in the mesentery above. It is probable that counter pressure posteriorly from the bodies of the vertebrae or aorta and from a wide ligament of Treitz above aided obstruction.

The common bile duct was slightly dilated above its outlet. The largest circumference measured 2 cm. The pancreatic duct joined the common duct within the duodenal wall. The ampulla was small and could not be easily probed.

The jejunal flexure was several centimeters distal to the duodenojejunal junction, perhaps due to the transverse position of the jejunum from the anastomosis. There was no evidence of any obstruction, narrowing or angulation at this flexure, even with considerable downward traction on the jejunum.

The microscopic examination of the duodenum showed no pathologic changes. There was no evident hypertrophy of the wall proximal to the crossing of the mesentery as compared to that segment under it and that, distally, The outer muscle layer remained constant in width while the inner circular muscle layer was increased slightly in width, respectively, from above downward.

The duodenum, which had been partially split open, was carefully sutured and distended with barium.

Roentgenograms showed a fairly well filled duodenum, except for the first portion which was somewhat distorted, due to postmortem shrinking. The descending portion was the largest. There was some narrowing evident at the mesenteric root. The duodenojejunal flexure was well distended and appeared to offer no opportunity for stasis at this time. The flexure was seen to be definitely in the jejunum, and beyond the terminal fixed point of the duodenum.

Two other cases of hyperthyroidism showed mild duodenal stasis, one associated with high grade stomach retention.

CASE 2.—*History.*—F. W. A., a man, aged 62, complained of weakness, loss of appetite, loss of 47 pounds (21.3 Kg.) in weight and a vague abdominal distress with considerable colicky pains and constipation. The abdominal distress was present the last five weeks, and he had eaten and drunk little since then. The diagnosis was primary exophthalmic goiter with mild duodenal stasis.

Examination.—The roentgenologic examination of the stomach showed a rather persistent stasis with considerable dilatation of the second portion of the duodenum. The basal metabolic rate was plus 44. The patient was given compound solution of iodine and medical treatment, with relief from abdominal symptoms. The superior thyroid arteries were ligated, and two months later a subtotal thyroidectomy was done. Ten days later, on fluoroscopic examination, there was observed prompt filling of the duodenum with a slight delay in the second portion. An occasional rush peristalsis carried the barium into the jejunum, alternating

with moderate reverse peristalsis. Three months later, the patient had gained 35 pounds (15.9 Kg.) and had no complaints. The patient was well on examination one year later.

CASE 3.—*History.*—A. D., a woman, aged 40, had a condition which was diagnosed as gastric and duodenal stasis with adenomas of the thyroid gland and mild hyperthyroidism. An attack of abdominal pain without vomiting had occurred one day previously. Recent less severe similar attacks were usually associated with constipation. A goiter with several palpable adenomas had been observed one year previously. She had been under medical care ever since. There was a history of spastic colitis.

Examination.—Roentgenologic examination of the colon gave negative results except for a moderate spasm in the descending and sigmoid portions. The stomach filled readily, with good peristaltic waves which closed off completely to the end of the antrum. The pylorus was slow in opening, and then the duodenal cap filled well. There was some stasis in the second portion of the duodenum and reverse peristasis. Four hours later, three fourths, and twenty-four hours later, one half, of the barium was still in the stomach. At these times the duodenal cap was filled, but the remaining portion of the duodenum was empty.

The basal metabolic rate was plus 13. The patient was treated by medical management for the abdominal distress with gradual improvement. One month later fluoroscopic examination of the stomach showed slightly delayed emptying with moderate reverse peristalsis in the second portion of the duodenum. One-half hour later the stomach was half empty and the duodenum was emptying normally into the small intestine. The abdominal symptoms were apparently largely relieved by medical management, and no acute exacerbations were noted in the subsequent year.

I have made roentgenologic examinations in several other cases of acute hyperthyroidism in which the patients have persistently vomited or have had abdominal pains. In these cases there was no evidence of duodenal or gastric dilatation or obstruction. The entire colon was spastic in a few cases.

Only two cases are classified in the literature as chronic duodenal ileus in which hyperthyroidism was noted. Neither case, however, may be considered one of classic duodenal ileus. Wilkie [1] reported a case of exophthalmic goiter with persistent bilious vomiting for three months. The roentgenograms showed calcareous tuberculous glands in the root of the mesentery, which it was thought contributed to the obstruction. The duodenal dilatation had not been great, and the observer thought that the duodenojejunostomy which he had done was probably not indicated and possibly had aggravated the thyrotoxicosis, since the patient died of a subsequent thyroidectomy while still in the hospital.

Higgins [2] reported one case with recent hyperthyroidism showing obstructive symptoms over several years. There was no vomiting, but nausea and regurgitation with loss of 20 pounds (9 Kg.) of weight

1. Wilkie, D. P. D.: Chronic Duodenal Ileus, Am. J. M. Sc. **173**:643 (May) 1927; Brit. J. Surg. **9**:204, 1921.

2. Higgins, C. C.: Chronic Duodenal Ileus, Arch. Surg. **13**:1 (July) 1926.

during the preceding year. There was gastroptosis and marked dilatation of the duodenum. Following thyroidectomy, the dilatation of the duodenum improved with the patient under medical treatment. Higgins reported four cases of duodenal ileus in which the patients had nontoxic goiters. Two of these were relieved by a duodenojejunostomy and two with medical treatment, but the dilatation was not great. In Wilkie's case the vomiting may have been due to the hyperthyroidism, rather than to the obstruction of the duodenum.

GENERAL CHARACTERISTICS

Etiology.—Chronic idiopathic duodenal ileus is more common in women. The most characteristic point of obstruction usually occurs at the crossing of the superior mesenteric artery in the root of the mesentery of the small intestine, although obstruction may occur at any point on the duodenum. The true idiopathic type is characterized by the inability to determine any pathologic cause, even at postmortem examination.

Congenital abnormalities and acquired intrinsic or extrinsic pathologic changes of the duodenum are fairly common and clinically it is difficult to differentiate a pathologic from an idiopathic obstruction.

Congenital atresia, or compression of the lumen by anomalous bands or blood vessels may occur in any part of the duodenum. Jackson [3] reported a case of partial obstruction in the second part due to a remnant of the anterior mesogastrium. Devine [4] reported the occurrence of megaloduodenum in children. Bakay [5] reported a case of obstruction by a Treitz hernia. The Kelloggs [6] mentioned obstruction due to hypertrophy of the valvulae of Ochsner's muscle, from inflammation and new growths.

There are numerous reports of cases of extrinsic pathologic changes producing obstruction. Postoperative obstruction has been observed due to a kinking of the duodenojejunal angle (Brown et al.[7]) or a localized peritonitis (Duval [8]) following gastrojejunostomy.

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3. Jackson, R. H.: Congenital Constriction of the Duodenum Due to an Abnormal Fold of the Anterior Mesogastrium, Ann. Surg. **84**:723 (Nov.) 1926.

4. Devine, H. B.: Basic Principles and Supreme Difficulties in Gastric Surgery, Surg. Gynec. Obst. **40**:1 (Jan.) 1925.

5. Bakay, L. V.: Disturbances of Passage in the Duodenum, Arch. f. klin. Chir. **141**:135 (May 22) 1926.

6. Kellogg, E. L., and Kellogg, W. A.: Chronic Duodenal Stasis, Radiology **9**:23 (July) 1927.

7. Brown, G. E.; Eustermann, G. B.; Hartman, R. H., and Rowntree, L. G.: Toxic Nephritis in Pyloric and Duodenal Obstruction: Renal Insufficiency Complicating Gastric Tetany, Arch. Int. Med. **32**:425 (Sept.) 1923.

8. Duval, P.; Roux, J. C.; Gatellier and Montier: Relations entre l'état infectieux des parois gastriques et certains troubles consecutifs a la gastro-enterostomie, Bull. et mém. Soc. nat. de chir. **52**:270, 1926.

There are two chief theories in the production of the idiopathic type of obstruction in the terminal duodenum, the mechanical and the neuromuscular. The mechanical type of marked idiopathic obstruction with hyperperistalsis is an unusual condition. Undoubtedly, fewer cases would be so classified if postmortem studies were made. Hyperperistalsis may be observed under the fluoroscope, and occasionally it is visible after the intake of fluids. This is the characteristic chronic type of duodenal ileus, but cases with a pathologic basis for duodenal stasis are reported under this classification.

The most commonly accepted belief is that obstruction of the terminal duodenum is due to pressure from the superior mesenteric artery.

At operation, Devine observed that the dilatation stops at the point of crossing of the superior mesenteric artery. Wilkie relieved the dilatation by lifting up the drag on the root of the mesentery.

Halpert [9] stated the belief that acute and chronic duodenal obstruction have the same etiology. In a study of the anatomy, he has concluded that pressure is caused by traction due to displacement of the small intestine into the pelvis, and that while jejunal branches of the superior mesenteric artery lie between the leaves of the mesenteric fold, they do not cause the obstruction. He located the point of obstruction on the pars horizontalis inferior just proximal to the ascending portion and some distance from the duodenojejunal flexure.

He found that the angle between the superior mesenteric artery and the aorta was at the level of the first lumbar vertebra, whereas the part of the duodenum at which obstruction occurs was at the level of the third lumbar. He found that the left renal vein may be compressed in this angle beneath the artery but never the duodenum. Clinically, he differentiated a primary arteriomesenteric occlusion followed by paralysis and passive dilatation of the stomach and a secondary dilatation of the duodenum following that of the stomach.

The relation of the origin of the root of the mesentery either to the right or to the left of the lumbar vertebra may influence obstruction. Snitzler [10] believed that obstruction was more likely when the ligament was attached to the right of the median line. Case [11] observed in the supine position that pressure of the vertebrae against the normal duodenum will sometimes cause obstruction at the "duodenojejunal flexure," with writhing duodenal movements. He also observed that if the

9. Halpert, B.: The Arteriomesenteric Occlusion of the Duodenum: An Anatomical Study, Bull. Johns Hopkins Hosp. **38**:409, 1926; Virchows Arch. f. path. Anat. **244**:439, 1923.

10. Snitzler, quoted by Stavely: Surg. Gynec. Obst. **11**:288, 1910.

11. Case, James T.: Chronic Obstruction of the Small Intestine, Bull. Battle Creek Sanit. & Hosp. Clinic. **22**:193 (Sept.) 1927; Radiology **9**:1, 1927.

patient had been resting on his right side preceding the roentgenologic examination, the duodenum was usually more than normally distended.

The development of the duodenum is separate from the small intestine as described by Hunter.[12] He observed, first, the formation of two loops in the straight duodenum; second, the rotation of the colon and changes in the adjacent viscera and, finally, the disappearance of the mesentery with the duodenum assuming its retroperitoneal position. The loop is formed before the development of the pancreas and is not molded by it.

Dwight [13] in a study of adult types of duodenum found that the primitive form is ring-shaped from which all others arise, and on relaxation it tends to resume this shape. On distention he found the U- and V-shapes most common; others were C-shaped or indeterminate. The superior flexure was usually at the level of the first lumbar vertebra and the lowest point of the descending portion decidedly lower than usually reported, usually opposite the fourth lumbar. The statement that usually the third portion crosses the aorta presumably with no peritoneum intervening and that the fourth portion ascends on its left, he found incorrect. He observed in fifty-four instances that the third portion crossed the aorta only eleven times, the fourth portion crossed it thirty-seven times, and the duodenum was entirely on its right side six times. In many cases in which the duodenum lay in front and in some to the left of the aorta, a fold of peritoneum lay between. It was difficult for Dwight to determine whether the original attachment of the mesentery was at the right or left of the aorta, but he believed it was along the right with intervening peritoneum frequently present. Halpert stated that the muscle of Treitz holds the terminal duodenum in position. However, Jonnesco [14] admitted that the fourth part slides easily and is less firmly attached than the second or third parts. Abnormal fixation of the terminal part has been suggested as the cause of obstruction.

Dwight found that the first part of the duodenum in man was egg-shaped and smooth and that the other parts presented irregular folds, especially the second. The largest circumference was usually in the second or third part. In two cases it was abnormally large, measuring 18 cm. in the second part.

The duodenum has been divided by Huntington [15] into a supramesocolic and an inframesocolic part by the root of the mesocolon. The

12. Hunter, R. H.: Development of the Duodenum, J. Anat. **61**:206 (Jan.) 1927.

13. Dwight, T.: Notes on the Duodenum and the Pylorus, J. Anat. & Physiol. **11**:517, 1897.

14. Jonnesco, quoted by Dwight (footnote 13).

15. Huntington, G. S.: The Anatomy of the Human Peritoneum and Abdominal Cavity, Philadelphia, Lea Brothers & Company, 1903.

inframesocolic part is further divided by the root of the mesentery of the small intestine into the pars inframesocolica dextra and sinistra.

Obstruction of the terminal duodenum by prolapse of a part or all of the colon has been described. Bloodgood,[16] however, believed that the prolapsed cecum pulled on the mesentery of the small intestine and that duodenal obstruction resulted when the last portion of the ileum had a short mesentery. He obtained relief in a few cases by resection of the right half of the colon. Traction of the cecum or ascending colon on the mesocolon may also press on the second part of the duodenum (Quain,[17] Duval, Kellogg and Kellogg) forming an arteriomesocolic type which must be differentiated from the arteriomesenteric type of terminal duodenal obstruction.

The Kelloggs have mentioned traction on the superior mesenteric artery by the pull of the prolapsed cecum on the ileocolic artery. They found that the prolapse of the transverse colon may also cause compression when the colic artery is given off above the duodenum or by a pull on the superior mesenteric artery itself. Wilkie, Duval and Gregoire[18] reported a case of obstruction by a right colic artery crossing the duodenum vertically. The Kelloggs observed obstruction due to an arterial anastomosing branch between the right colic and the middle colic arteries.

Duodenal obstruction by prolapse of the stomach has been described. The Kelloggs stated the belief that gastroptosis increases the acuteness of the superior duodenal flexure and that obstruction may occur either at the inferior duodenal flexure, the mesenteric root or at the duodenojejunal flexure. Bakay described compression of the duodenum by the lesser omentum in gastroptosis. De Luna[19] observed obstruction in the first and second portion in gastric ptosis. Adams[20] stated that a kink usually occurred at the duodenojejunal flexure but occasionally at the junction of the first and second parts of the duodenum. He believed that a duodenojejunal kink is due to the drag of a ptosed stomach on the first part of the duodenum, which pulls it around the head of the pancreas until it is held at the duodenojejunal angle.

Recently the Kelloggs have reported compression of the jejunum at the pelvic brim by prolapse of the small intestine into the pelvis as a new cause of duodenal stasis.

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16. Bloodgood: Dilatation of the Duodenum in Relation to Surgery of the Stomach and Colon, J. A. M. A. **59**:117 (July 13) 1912.

17. Quain, E. P.: Periduodenitis, Minnesota Med. **9**:431 (Aug.) 1926; Am. J. Surg. **38**:198, 1924; Pathogenic Ptosis of Right Colon, Arch. Surg. **6**:638 (April) 1923.

18. Gregoire, quoted by Wilkie (footnote 1).

19. De Luna, C.: Le syndrome duodenal dans la ptose gastrique, Marseilles méd. **63**:1261 (Aug. 15) 1926.

20. Adams, J. E.: Duodenal Ileus, Brit. J. Surg. **14**:67 (July) 1926.

Ptosis of the right kidney, tumors, pressure from the pancreas, aneurysm and infection in the gastric wall and perigastric lymphatics (Duval) may be factors in duodenal obstruction.

The neuromuscular type of duodenal obstruction may occur either from increased contraction or from paralysis of the duodenal musculature. This theory is advocated by Robertson and Devine who question the mechanical theory because of failure to relieve the symptoms in a number of cases by short circuiting operations. Some failures have been reported by others. However, in the absence of a thorough anatomic or postmortem study, any comparison of medical and surgical treatment in the varied types of stasis classified as chronic duodenal ileus is unreliable. Robertson [21] believed that the obstruction is due to a disturbance of nerve balance between the vagi and the sympathetic. He stated that either stimulation of the sympathetic or a depression of the vagi may result in dilatation. Devine stated that the sympathetic tonus aids retention in the stomach and duodenum. The function of the parasympathetic is to empty the viscus and it acts intermittently, the two systems being complementary. He considered duodenal ileus as an exaggerated retention similar to cardiac spasm due to neuromuscular derangement above the duodenal rudimentary sphincter. Alvarez [22] experimentally found that both the vagus and splanchnic nerves serve as inhibitors and regulators of intestinal activity. The only sign of antagonism was found in conduction, which was improved by vagotomy and injured by splanchnicotomy.

Carlson,[23] Bolton and Salmond [24] considered antiperistalsis of the duodenum as a normal condition for the purpose of mixing food with the digestive juices. Glenard [25] believed that physiologic retention in the duodenum was produced by pressure on the duodenum by the mesenteric ligament.

The action of morphine and opium on the duodenum and intestinal tract is of interest in my case because of the large continued doses given

21. Robertson, G.: Acute Dilatation of Stomach and Intestinal Tube with Consideration of Chronic Duodenal Ileus, Surg. Gynec. Obst. **40**:206 (Feb.) 1925.

22. Alvarez, W. C.: The Effects of Degenerative Section of the Vagus and the Splanchnic Nerves on the Digestive Tract, Proc. of the Staff Meetings of the Mayo Clinic **4**:205 (July 3) 1929.

23. Carlson, A. J.: Movements of the Alimentary Tract in Experimental Animals, Illinois M. J. **55**:429 (June) 1929.

24. Bolton, C., and Salmond, R. W. A.: Antiperistalsis of Duodenum and Its Relation to Pyloric Regurgitation, Lancet **1**:1230 (June 11) 1927. Salmond: Observations on the Movements of the Duodenal Contents with Special Reference to Antiperistalsis and Pyloric Regurgitation, Proc. Roy. Soc. Med. **21**:1361 (June) 1928.

25. Glenard, quoted by Stavely (footnote 31).

during the persistent delirium and during the onset of the ileus. Weitz and Vollers [26] found that opium increases the tonus of the stomach and intestines. There was an increase of the pendulum movements of the intestine, which they thought might favor the resorption of fluids and account for the constipating action of the opium. Recently I studied roentgenologically the case of a man, aged 44, who had been a morphine addict for ten years. The stomach was normal. The duodenum filled well and emptied normally, but there was occasional antiperistalsis with slight puddling. The colon was normal except for a moderate spastic condition throughout.

Hypertonicity may have been a factor in the duodenal obstruction in my case and also in the diarrhea which occurred with each aggravation of duodenal obstruction. However, the administration of morphine and opium was discontinued before the last and worst attack of obstruction. Hypertonicity might have initiated an obstruction which easily became a mechanical, valvelike, obstructing angulation of the duodenum at the crossing of the mesentery. Higgins stated that hyperperistalsis was present in marked cases of duodenal ileus which required short circuiting operations.

Pathologic Changes.—The anatomic changes reported previously in chronic idiopathic duodenal ileus have been limited apparently to observations under the roentgen ray and at operation. At operation, Wilkie frequently observed a bulging of the first part of the duodenum with the stomach dilated and the pylorus patent. On lifting up the transverse colon, he observed that the small intestine was usually in the pelvis and that the third part of the duodenum was usually dilated. Others have reported dilatation up to the point of crossing the superior mesenteric artery.

A plastic exudate about the superior duodenojejunal fossa has been described by Miller [27] and must be differentiated from the changes such as may occur in a localized peritonitis following a gastrojejunostomy or associated with a gastric ulcer. Wilkie stated that there was usually a lack of hypertrophy of the muscle wall in chronic duodenal ileus but that it might occur. Devine rarely found evidence of it. The Kelloggs stated that there was first hypertrophy and hyperperistalsis with late atrophy, dilatation and stasis. They noted that the pylorus was at first hypertrophied and spastic, later becoming incompetent.

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26. Weitz, W., and Vollers, W.: Ueber die Beeinflussung der Bewegungen des Magens und Darms durch Opium, Ztschr. f. d. ges. exper. Med. **54**:161 (Jan. 25) 1927.

27. Miller, E. M., and Brown, R. C.: Chronic Duodenal Ileus, S. Clin. North America **5**:1117 (Aug.) 1925.

From roentgenographic examinations, the Kelloggs have described four types of duodenal stasis:

1. The asthenic duodenum in which symptoms were latent or toxic. Roentgen examination showed delay or puddling in the duodenum, with sluggish peristalsis and slight or no dilatation.

2. Duodenal obstruction with an incompetent pylorus. The dilatation of the stomach was moderate or absent. The roentgenologic examination of the duodenum gave negative results or occasionally showed reverse peristalsis.

3. Duodenal obstruction with hypertrophy. The duodenum was elongated and its walls were thickened. Under the fluoroscope it was seen to labor over its contents (writhing duodenum). Cramplike pains were common.

4. A dilated duodenum. The area of tympany was increased and pain was steady or cramplike. This type was most readily demonstrated by the roentgen examination.

There was practically complete obstruction in my first case under the fluoroscope, but there was a slight passage of barium on turning the patient to the left side and in the prone position. This together with hyperperistalsis would speak for a mechanical nonstrangulating type of obstruction.

The duodenal stasis in my other cases was of a mild type; in case 2 reverse peristalsis was still observed after thyroidectomy.

Experimentally, Berg et al.[28] have produced a persistent duodenal obstruction in dogs which should not be compared to the clinical idiopathic ileus because the latter may act intermittently. These authors obtained a dilatation and hypertrophy above the obstruction with emaciation, but there were no symptoms of intoxication. They usually found bacteria present. After partial obstruction, bacteria especially of the colon group increased, but later they occasionally decreased. Usually fewer organisms were found below the obstruction.

The anatomic type predisposing to duodenal obstruction has been described as spare and slender having a narrow costal angle and a broad pelvis.

Associated Pathologic Processes.—Associated ulcers of the stomach and duodenum have been reported (Ryle[29]). Wilkie believed that the duodenal obstruction predisposed to ulcers. He found among seventy-five cases, four patients with gastric ulcers and three with both gastric and duodenal ulcers.

In cases of pathologic duodenal and pyloric obstruction, especially cases in which tetany resulted, toxic nephritis has been observed by

28. Berg; Meleney and Jobling: Experimental Chronic Duodenal Obstruction, Technic and Physiology, Arch. Surg. **14**:752 and 770 (March) 1927.

29. Ryle, J. A.: Case of Duodenal Ileus with Perforating Duodenal Ulcer, Guy's Hosp. Rep. **76**:162, 1926.

Brown and others. Associated lesions of the pancreas and gallbladder, some with jaundice, have been reported. Hyperthyroidism may be associated.

Symptoms.—Chronic duodenal ileus is usually remittent or intermittent. The clinical symptoms may be vague or characteristic. They may date back to childhood or appear in adult life, especially following an emaciating illness or childbirth.

Pain is the most distressing symptom. Wilkie found that it usually occurs one-half hour after meals. It may be at the left or the right of the umbilicus. Epigastric fulness and flatulence are common after meals.

Vomiting of large amounts is usually present but occurs periodically. Wilkie observed it lasting from one to two days about every four to five weeks. It may occur at certain periods each day, frequently several or even many hours after a meal. The fluid is usually bile colored. There is often a dread of eating.

Loss of weight during the acute attacks may be rapid, with alarming dehydration. There may be tetany-like manifestations. The attacks are often described as bilious. They are often associated with headache, malaise, depression and neuralgia.

Toxic symptoms somewhat similar to uremia and shock have been described, but I have not noted previous reports of changes in the blood chemistry in the idiopathic type. In extensive pathologic obstruction of the duodenum, examinations of the blood chemistry have shown (Brown and others) a low level of chlorides, a high level of blood urea and of creatine and a high carbon dioxide carrying capacity.

It is significant that no changes were observed in the blood chemistry in my case during the acute exacerbations with persistent vomiting and loss of weight.

In experimental partial duodenal obstruction by Berg and his co-workers, there was also an absence of intoxication even though it produced dilatation with hypertrophy. Clinically, in acute intestinal obstruction and ileus, McVicar and Weir [30] found severe toxemia with dehydration before the occurrence of disturbances in the blood. Changes in the blood chemistry should therefore speak for pathologic changes such as a high grade stenosis from new growth or adhesions. However, acute dehydration, vomiting and emaciation may be present in either idiopathic or pathologic obstruction.

On physical examination in duodenal obstruction, the patient is usually found to be thin and may be emaciated. Tenderness may be present near the umbilicus. Distention and fulness may be marked.

30. McVicar and Weir: Nature and Treatment of the Toxemia of Intestinal Obstruction and Ileus, J. A. M. A. **92**:887 (March 16) 1929.

The stomach may be low and dilated. The observation of a huge distended duodenum filling almost the entire abdomen and extending below and to the left of the normal location, with visible peristaltic waves as in my case is apparently rare. Wilkie has described a definite tympanic swelling of the duodenum in one case as unusual.

Haye's procedure of pressure upward and backward may demonstrate gas gurgling through the duodenum. The Cash symptom of duodenal splashing or succussion was occasionally observed by Kellogg and rarely by Wilkie.

PROGNOSIS AND TREATMENT

The prognosis will depend on the recognition of the various factors involved in the idiopathic as well as in the pathologic obstruction with the institution of appropriate treatment. In a well developed obstruction of the terminal duodenum, with hyperperistalsis, a duodenojejunostomy is usually indicated. However, the latter may not give complete relief when there are pathologic changes or neuromuscular disturbances involving other portions of the gastro-intestinal tract.

Obstruction of the proximal duodenum by anomalous bands or adhesions should be excluded. Quain has obtained good results by means of a transmesocolic duodenojejunostomy. The bands may occasionally be divided; a gastrojejunostomy may also give relief, although it usually does not when obstruction is in the terminal duodenum (Adams). Resection of the colon as performed by Bloodgood is rarely necessary for any type of duodenal obstruction.

In a study of the late results in fifty-seven cases classified as chronic duodenal ileus, Wilkie found twenty-three patients cured, eleven improved, twelve still having slight symptoms and nine without relief. The last group included the cases of visceroptosis. He found the best results in cases with roentgenographic evidence of dilatation and no evidence of mechanical obstruction. In thirty cases in which the patients were treated by duodenojejunostomy alone, the Kelloggs found eighteen free from symptoms and nine improved. There were two deaths in a total of seventy-seven patients treated by duodenojejunostomy alone or combined with other procedures.

A lateral anastomosis of a loop of jejunum to the second portion of the duodenum as suggested by Barker and performed by Stavely [31] is usually the operation of choice in obstruction near the terminal duodenum. The stomach and duodenum should be aspirated if necessary before operation. It is unnecessary to use a clamp on the duodenum or the jejunum.

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31. Stavely, A. L.: Chronic Gastromesenteric Ileus, Surg. Gynec. Obst. **11**: 288, 1910.

The usual technic for a lateral anastomosis is satisfactory. The use of an outer row of fine silk or linen sutures is advisable, with additional sutures to prevent angulation of the jejunum. Some other operative procedures may be indicated when duodenal ileus is associated with anatomic or pathologic conditions.

SUMMARY AND CONCLUSIONS

In case 1 the following observations were made:

1. The stomach and pylorus were dilated together with the duodenum, and there was hyperperistalsis with a churning back and forth in the duodenum before operation.

2. There was no unusual ptosis evident in the stomach or duodenum, except that resulting from dilatation.

3. There was a subsidence of duodenal dilatation after operation.

4. At postmortem examination, the descending and inferior portions of the duodenum were widest proximal to the root of the mesentery. There was a narrowed segment beneath the mesentery containing the superior mesenteric blood vessels.

5. The ampulla of Vater was apparently continent.

6. A pull on the mesentery itself did not seem to produce a narrowing of the duodenal lumen.

7. The superior mesenteric artery crossed the duodenum about 4 cm. from the duodenojejunal junction. A downward pull on this artery easily produced obliteration of the duodenal lumen beneath it.

8. There was no evidence of hypertrophy of the duodenal wall either at operation or at postmortem examination.

9. The ligament of Treitz was broad at its insertion. This band might have hypertrophied and increased the fixation of the duodenum, or it might have aided counterpressure against the superior mesenteric artery.

10. It seemed impossible by downward or lateral traction on the jejunum, by pulling on the ligament of Treitz or by distention of the duodenum to produce any narrowing of the lumen or kinking at the duodenojejunal flexure.

Factors arising from acute hyperthyroidism that may have favored duodenal obstruction were a suddenly increased fluid intake, emaciation, rigidity and retraction of the abdominal muscles, irritable colon with diarrhea, constant lying on the right side, cardiac decompensation, a neuromuscular disturbance perhaps aggravated by large doses of morphine and opium and delirium.

A congenital origin, the standing position, inflammation of the gallbladder and the presence of pathologic changes or anatomic anomalies

may be eliminated as factors in this case. Probably after a certain amount of distention, a mechanical valve forms under the root of the mesentery and in turn aggravates the contributing factors.

Marked hyperperistalsis may occur with a huge dilatation of the duodenum of several weeks' duration, and the lumen may return almost to its normal size shortly after duodenojejunostomy with little evident hypertrophy of the wall.

Chronic nephritis may result, but changes in blood chemistry such as observed with marked pathologic obstruction or stenosis of the duodenum do not necessarily occur. Severe hyperthyroidism may not act directly in the causation of duodenal obstruction, but undoubtedly it may contribute to its development.

Chronic idiopathic obstruction of the terminal duodenum with dilatation is a clinical entity and pathologic changes are not necessarily present. Abnormal or variable anatomic factors may aid obstruction in conjunction with a number of functional and neuromuscular disturbances which may be the activating factors. The most necessary factor in the obstruction is probably pressure by the superior mesenteric artery together with the root of the mesentery. Traction on this artery may be produced, clinically, by pelvic displacement of the small intestine.

TUBERCULOUS PERITONITIS

A STATISTICAL AND CLINICAL STUDY OF ONE HUNDRED AND EIGHTY-SEVEN CASES *

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Although there are numerous monographs and countless shorter articles on the subject of tuberculous peritonitis in the literature, there are relatively few contributions that deal with the disease exclusively as it affects women and in its relation to gynecological conditions. It has been thought worth while, therefore, to give some consideration to this subject, and we have chosen as our means of doing so a statistical study of all patients with proved cases of tuberculous peritonitis treated on the gynecological service of the Johns Hopkins Hospital from its opening on May 7, 1889, until June 30, 1927. In pursuing this study, we have attempted to analyze particularly the types of the disease, both clinical and pathologic, the methods of treatment and the ultimate results. The study of results has not been entirely satisfactory, owing to many difficulties encountered in tracing the subsequent course of patients after their discharge from the hospital. We have, however, obtained data sufficient to admit of some relatively sound conclusions.

HISTORICAL DATA

It was not until the advent of modern surgical methods had led to frequent laparotomies that anything like an adequate idea of the frequency of tuberculous peritonitis and of its various clinical and pathologic manifestations was reached. The condition had been described in isolated instances as far back as the eighteenth century, Morgagni [1] having published the first satisfactory description of a case in 1744. Two other cases, one by Johnson in 1779, and another by Walther in 1785, were reported in this century, and in the first half of the nineteenth century the pathologic anatomy was described by many of the workers on tuberculosis in general (Bichat, Laennec, Boyle, Louis).[2] During this period, the disease was considered invariably fatal.

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1. Morgagni: De sedibus et causis morborum, epistola 38, no. 34, ed. Radius.
2. Clavier, Lucien: Thèse de Paris, 1895.

As early as 1862, Sir Spencer Wells [3] performed a laparotomy on a young woman, aged 22, who was believed to have an ovarian tumor. He found a typical picture of tuberculous peritonitis of the ascitic type, removed the fluid and closed the abdomen. The patient recovered and was well twenty-years after the operation. In 1884, König [4] reported a series of 4 cases in which operation was performed with 3 recoveries; he proposed laparotomy as the method of treatment as soon as the diagnosis should have been made. In 1887, Kümmel [5] reported 40 cases with operation and, in 1890, König [6] collected and presented at the Congress of Surgeons in Berlin the cases of 131 patients who had been treated by laparotomy. In this series, there was an apparent cure in 84, or 65 per cent of the cases, but in only 30 of them had a period of two years or more elapsed since the operation.

In this country, Van de Warker,[7] in 1887, was the first to advise laparotomy as a method of treatment. He concluded: "It is safe to assume that opening the abdomen in instances of tuberculous degeneration of its lining membrane is comparatively free from danger, and, in view of its possible benefit, amply justified."

Thus, surgical intervention gave a tremendous impetus to the study of this disease. In the next few years, many series of cases were reported with the results from operative treatment. In 1892, Lindner reported 205, and Aldibert 308 cases. The following year Roersch collected 358 and Adossidies 405 cases. In 1896, Margarucci collected 253 cases of patients operated on by members of the Italian Surgical Society, showing 216 instances, or 85.4 per cent, of cures.[8] Besides the reports of surgical treatment, general consideration of the disease became the subject of numerous studies. Several theses for the degree of Doctor of Medicine at the University of Paris [9] were devoted to the

3. Wells, Sir Spencer: Diagnosis and Surgical Treatment of Abdominal Tumors, London, J. & A. Churchill, 1885, p. 210.

4. König, F.: Ueber diffuse peritoneale Tuberkulose und die durch solche hervorgerufenen Scheingeschwülste im Bauch nebst Bemerkungen zur Prognose und Behandlung dieser Krankheit, Centralbl. f. Chir. **11**:81, 1884.

5. Kümmel, H.: Ueber Laparotomie bei Bauchfelltuberkulose, Arch. f. klin. Chir. **37**:39, 1888.

6. König, F.: Die peritoneal Tuberkulose und ihre Heilung durch den Bauchschnitt, Centralbl. f. Chir. **17**:657, 1890.

7. Van de Warker, Ely: Laparotomy as a Cure for Tuberculosis of the Peritoneum, Am. J. Obst. **20**:932, 1887.

8. Johnston, George B., in Kelly and Noble: Gynecology and Abdominal Surgery, Philadelphia, W. B. Saunders Company, 1914, vol. 2, p. 617.

9. Alleaume, G.: Thèse de Paris, 1894. Guillemare, G.: Thèse de Paris, 1898. Lichteman, S.: Thèse de Paris, 1896. Clavier (footnote 2).

subject, and in Germany monographs were contributed by Cramer,[10] Lauper[11] and Strassburg.[12]

In America in 1890, Osler,[13] published a monograph describing the various clinical and pathologic types of the disease, and, in 1903, Murphy[14] included in a monograph on tuberculosis of the female genitalia a rather complete description of the disease as it occurs in women.

Since 1900, the volume of literature has increased rapidly, and it would seem that any merely statistical addition might be superfluous. We find, however, that the subject in its relation to gynecology alone has not been dealt with thoroughly enough to render valueless a few additional statistics. We offer, therefore, the following study of 187 cases as a contribution to the gynecological aspect of tuberculous peritonitis.

TABLE 1.—*Incidence of Tuberculous Peritonitis*

Time Periods	Patients Treated			Patients with Tuberculous Peritonitis			Percentage Incidence		
	White	Colored	Total	White	Colored	Total	White	Colored	Total
May 7, 1889 to Jan. 31, 1900....	5,614	935	6,549	30	11	41	0.54	1.18	0.63
Feb. 1, 1900 to Jan. 31, 1909....	6,814	1,990	8,804	33	25	58	0.48	1.26	0.66
Feb. 1, 1909 to Jan. 31, 1919....	6,164	2,989	9,153	22	21	43	0.36	0.70	0.47
Feb. 1, 1919 to June 30, 1927....	5,009	3,489	8,498	12	33	45	0.24	0.95	0.53
Total—May 7, 1889-June 30, 1927	23,601	9,403	33,004	97	90	187	0.41	0.96	0.56

OBSERVATIONS ON ONE HUNDRED AND EIGHTY-SEVEN CASES

Incidence.—Table 1 is a composite table showing the incidence of tuberculous peritonitis on the gynecological service of the Johns Hopkins Hospital as distributed between the white and colored races and for the different decades since the opening of the hospital in 1889.

It will be seen from this table that the incidence for the entire period has been 0.56 per cent. As compared with the general statistics gathered from the literature, this is a remarkably low figure, but it must be taken into consideration that most of the statistics found in the literature are compiled from autopsy rather than from clinical records, and still further that only those women in whom the peritonitis is definitely associated with tuberculosis of the pelvic organs are admitted to the

10. Cramer, C.: Ein Fall von Bauchfeltuberkulose, Berlin, G. Schade, 1895.

11. Lauper, J.: Beiträge zur Frage der Peritonitis tuberkulösa, Leipzig, J. B. Hirschfeld, 1901.

12. Strassburg, J. L. A.: Ueber Peritonitis tuberkulösa, Kiel, Schmidt & Klaunig, 1902.

13. Osler, William: Johns Hopkins Hosp. Rep. **2**:67, 1890.

14. Murphy, John B.: Tuberculosis of the Female Genitalia, Am. J. Obst. **48**:737, 1902; ibid. **49**:205, 1902.

gynecological service, the others being assigned to either the medical or the general surgical services. In the first 7,000 autopsies at the Johns Hopkins Hospital there were 197 cases of tuberculous peritonitis, or an incidence of 2.8 per cent. Engelmann [15] found that in 2,837 autopsies at the Munich Pathological Institute 1.6 per cent and that of 8,421 cases from the Berlin Pathological Institute during ten years 2.5 per cent of the patients had suffered from this disease. In Erlangen during twenty-three years, the autopsy records showed 1.5 per cent, and in Kiel 5,425 autopsies in fifteen years gave 1 per cent. These reports include only cases resulting fatally from tuberculous peritonitis. At the Pathological Institute of the University of Prague the statistics of 3,500 autopsies, including the incidental finding of tuberculous peritonitis, gave a percentage incidence of 4.7 per cent.[8] In this country, Cummings,[16] in 3,405 autopsies from the Pennsylvania, Philadelphia and University Hospitals, found 92 cases of tuberculous peritonitis (2.7 per cent).

Cummings further found tuberculosis in some form in 835 of the autopsies, or 24.5 per cent, and of these the 92 with peritoneal involvement constituted 11 per cent. In 1,170 autopsies at the Boston City Hospital, Bottomley [17] found tuberculosis in 197 or 16.8 per cent, and tuberculous peritonitis in 14 or 7.1 per cent of these. Nothnagel [18] said that statistics vary from 1.25 to 16.16 per cent of peritoneal involvement among tuberculous patients. He further stated that 24.8 per cent of all cases of peritonitis are tuberculous.

One other point of interest is to be derived from our statistics as presented in table 1, namely, the gradual decline in incidence during the period under consideration. This has been more striking among white than among colored patients. Among the colored patients, the most notable decline was during the third decade with a subsequent slight rise during the past eight years. In the literature we have encountered no similar statistics to compare with our own, which, however, are in accord with the figures on tuberculosis in general, which has shown a considerable decrease in incidence during the past forty years.

Sex.—Pathologic statistics usually show the disease to be more common in men than in women. Sixty-two of Cummings' [16] 92 cases were in males and 30 in females. In his own series of 21 patients Osler [18]

15. Engelmann, F. W.: Beiträge zur Kenntnis der Bauchfellentzündung, besonders der tuberkulösen Form, Diss., München, 1902, p. 34.

16. Cummings, W. T.: Univ. Penn. M. Bull. **18**:272, 1905-1906.

17. Bottomley, John T.: Am. Med. **3**:265, 1902.

18. Nothnagel: System of Medicine; quoted by Cummings: Univ. Penn. M. Bull. **18**:272, 1905-1906; quoted by Bottomley: Am. Med. **3**:265, 1902.

found that 15 were males, but he stated that the disease is more common in females, and from the combined figures of Boulland, Häne, Mourange and his own found a total of 60 males and 131 females. In Seik's series of 107 cases, 89 of the patients were males and 18 females. Johnston [8] stated that from the combined statistics of König, Lindner, Kümmel and Rosenburg (all surgeons) in 386 cases, only 36 of the patients were men while 350 were women. Thus there is a marked discrepancy between pathologic and operative statistics. As a possible explanation for this Johnston [8] offered that in most pathologic reports no account is taken of the relative number of total autopsies on males and females, and he was of the opinion that the males are usually in larger numbers. We would suggest further that the frequent association in females of peritonitis with tuberculosis of the generative organs and the resulting possibility of successfully extirpating the primary focus at operation lead to operative treatment far more frequently in females than in males, thus accounting for the discrepancy in the statistics on the other side. After reviewing all these statistics, one would be inclined to believe, therefore, that there probably is no very great difference in the incidence of the disease among the two sexes.

Race.—Osler [13] stated that it is generally believed that the disease is more common among the colored than the white race but that there are no statistics on the subject justifying any definite decision. Three of his 4 patients at the Johns Hopkins Hospital belonged to the colored race. We also, in reviewing the later literature, have found a striking paucity of figures on this subject. Of 77 cases reported by Cummings,[16] in which the race was stated, 39 were in colored and 38 in white patients; but Cummings gave no figures as to the relative frequency of white and colored in his total of autopsies. Our figures show a decidedly higher incidence among the colored patients. Of our 187 patients, 97 were white and 90 colored, but during the period under consideration there were 23,601 white patients treated on the service and only 9,403 colored patients, so that the incidence among white patients for the total period was 0.41 as compared with 0.96 per cent among colored patients. Greenberg,[19] in a review of 200 cases of tuberculous salpingitis from our service, found an incidence of 0.71 per cent among the white and 1.18 per cent among the colored patients. Thus our figures are in accordance with the general opinion that has been held, but without statistical confirmation as to the greater frequency among the colored race.

Age.—It is generally stated and confirmed by statistics that tuberculous peritonitis occurs with the greatest frequency between the ages of 20 and 40 years. Table 2 shows our figures on this subject as com-

19. Greenberg, J. P.: Johns Hopkins Hosp. Rep. **21**:100, 1924.

pared with some of the more representative ones collected from the literature.

All of the figures in table 2 illustrate clearly that we are dealing with a disease occurring most commonly in young adults. In our own series practically half the patients were between 20 and 30 and 170 of the 187 were between the ages of 10 and 40.

Parity.—Howard A. Kelly [20] stated that pregnancy has a definite causal relationship to tuberculous peritonitis. In 28 per cent of his cases the onset was definitely dated from a miscarriage or labor. He further stated that of the married women 29.41 per cent remained sterile, and 11.76 per cent miscarried every time; 41.17 per cent were

TABLE 2.—*Age Incidence of Tuberculous Peritonitis*

Age, Years	Authors' Cases		Osler's Cases Collected*		Cummings' Cases	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
Under 10	1	0.53	27	8	4	5
10 to 20	47	25.14	75	21.6	14	17.7
20 to 30	92	49.27	87	25.1	17	21.6
30 to 40	31	16.58	71	20.5	17	21.6
40 to 50	10	5.35	61	17.5	12	15
50 to 60	6	3.20	19	5.5	9	11.4
Over 60	0	0.0	6	1.8	6	7.6
Total	187	100	346	100	79	100

* Osler's cases consist of his own 21 combined with those of Boulland, Häne, Mourange, Fenwick, Bristowe, Hilton Fagge and Lebert.

TABLE 3.—*Number of Pregnancies Among the Ninety-One Parous Women with Tuberculous Peritonitis*

1 in 32	4 in 14	7 in 2	10 in 2
2 in 16	5 in 7	8 in 2	11 in 0
3 in 8	6 in 3	9 in 3	12 in 2

sometimes delivered at term and sometimes had miscarriages, while but 17.64 per cent always went to term.

In our series, there were 51 unmarried women and 136 who were or had been married; 87 were nulliparous; 91 had borne one or more children, and in the histories of 9 there was no statement in this regard. The number of pregnancies among the 91 women who had borne children is shown in table 3.

Only 10 of the women are recorded as having had abortions. In 27 cases, or 14.5 per cent, the onset occurred during or followed within a short time after the termination of a pregnancy, while in a parous woman who had had 7 pregnancies, the tuberculous peritonitis did not come on

20. Kelly, Howard A.: Operative Gynecology, New York, D. Appleton & Company, 1906, vol. 2, p. 237.

until nineteen years after the termination of the last one. Of the 27 in whom the onset was associated with pregnancy, in 6 the pregnancy ended in a miscarriage.

Contact.—The history of contact with tuberculous persons is absent in a strikingly large percentage of our patients. Only 38 gave a definite family history of tuberculosis, while 131 absolutely denied any ascertainable source of contact. In 18 histories there was no record regarding this point. In Kelly's [20] 16 cases there was a tuberculous family history in only 2. Bottomley [17] found a definite family history in only 2 of 25 cases. These figures are rather confirmatory of the accuracy of our own, about which, however, we are still inclined to some skepticism on account of the gross ignorance of many of the patients included in our series.

Symptomatology.—The disease presents great variations in its clinical manifestations, and in the degree of its severity. There are several definitely distinct pathologic varieties which we shall discuss

TABLE 4.—*Duration of Symptoms*

Less than 1 month.....17	7 months..... 3	3 to 4 years..... 6
1 month.....12	8 months.....11	4 to 5 years.....11
2 months.....12	9 months..... 9	5 to 6 years..... 3
3 months.....11	10 months..... 1	6 to 7 years..... 2
4 months.....15	11 months..... 4	8 years..... 1
5 months..... 6	1 to 2 years.....27	10 years..... 1
6 months.....13	2 to 3 years.....16	Questionable..... 6

later, and the symptoms and clinical course vary considerably with these forms. From a purely clinical point of view, regardless of pathologic changes, certain definite observations may be made.

In the first place, the onset may be sudden with severe symptoms of an acute illness which may terminate fatally or pass over into a chronic form. On the other hand, the onset may be insidious and symptoms may progress slowly so that months or even several years may elapse before the patient finally seeks medical assistance. In our series of cases, 73 patients had noticed their symptoms for a year or more when they first came to the clinic, while 114 suffered severely enough to induce them to seek aid within the first year. In 17 of these the symptoms were so acute as to bring them to the clinic within the first month after onset. Table 4 shows the duration of symptoms in the 187 patients at the time they first presented themselves at the clinic.

Osler [13] stressed the point that the symptoms may be quite latent and cited several cases in which the condition was discovered during the course of autopsies on patients who had died of an entirely different malady and in whose cases there had been no suggestion of a tuberculous peritonitis during life. On the other hand, he also stressed a

group of cases in which the onset is so sudden that the disease is apt to be confused with some condition more commonly acute, such as enteritis, hernia or simple acute peritonitis. In analyzing our cases according to the severity of symptoms and signs, it was found that 25 could be considered as acute, 31 subacute, 119 chronic, 7 as chronic with acute exacerbation at the time of admission and 5 as latent. These figures, together with those in table 4, seem to indicate clearly that in the majority of cases the disease runs a chronic course, while in a small minority the symptoms are those of an acute illness.

Later in this paper we shall classify our cases pathologically according to Murphy's [14] groups I, III and IV, omitting his group II. The three groups that we have found it convenient to use are: I, the disseminated, exudative, miliary, nonconfluent serous (ascitic) variety; III, the adhesive, fibroplastic, cystic, partition or obliterative variety, and IV, tuberculous peritonitis with mixed or secondary infection. In group I there are 42, in group III, 108 and in group IV, 12 cases. The remaining 25 cases could not be classified because of insufficient data due to the fact that in the majority no operation was performed. We have thought it worth while at this point to attempt a correlation between these pathologic groups and the several clinical varieties such as acute, chronic and latent. Accordingly, of the 42 cases in group I, 6 were acute, 7 subacute, 28 chronic and in 1 the process was entirely latent, giving rise to no symptoms whatever. Of the 108 cases in group III, 6 were acute, 14 subacute, 82 chronic and 3 chronic with an acute exacerbation. In group IV, those with secondary infection, all the patients were acutely ill. Thus it is seen that, with the exception of group IV, the great majority of cases are chronic regardless of the pathologic type, but that the percentage of acute cases in group I (14.3) is somewhat higher than that in group III (5.5). This is of some significance as it will be seen later that a case which in the early stages presents a picture characteristic of group I will later present the features of the more frequently chronic group III.

Chief Complaint.—In analyzing the chief complaint with which the patients presented themselves, it is found that in the vast majority of the cases pain in one form or another was the determining factor that brought the patient to the clinic. In fact, 161 of the 187 patients complained of some form of pain, usually located in the abdomen. A variety of other symptoms were also sufficiently annoying to be mentioned with the chief complaint. These were sometimes complained of alone but more often in association with pain. Table 5 gives the varieties as to character and location of the pain complained of, and in table 6 will be seen the various other more or less prominent symptoms.

There is little of diagnostic value to be learned from the facts presented in table 5. The types of pain complained of are such as

commonly accompany a variety of intra-abdominal conditions. Table 6, however, is somewhat more helpful, in that it shows abdominal swelling to be a symptom rather frequently observed by the patient. Abdominal swelling, particularly when it can be proved to be due to ascites, is strongly suggestive of one of several conditions: tuberculous peritonitis, cirrhosis of the liver, carcinomatosis, flaccid ovarian cyst, fibroma of the ovary associated with marked ascites or general anasarca due to cardiac or renal disease. All of these conditions except the first are apt to occur in persons of at least middle age. Our statistics, however, show tuberculous peritonitis to be far more common in younger per-

TABLE 5.—*Varieties of Pain Mentioned in Chief Complaint*

Abdominal pain	54	Headache	5
Lower abdominal pain	41	Drawing abdominal pain	2
Right lower quadrant pain	13	Pain around umbilicus	2
Backache	13	Shooting lower abdominal pain	1
Abdominal soreness	10	Pain in right hip	1
Left lower quadrant pain	5	Pain in left flank	1
Abdominal cramplike pain	5	Chest pain	1
Dysmenorrhea	5	Pain of various types; total	161

TABLE 6.—*Other Symptoms Mentioned in Chief Complaint*

Abdominal swelling	58	Diarrhea	2
Weakness or susceptibility to fatigue	13	Loss of weight	2
Nausea and vomiting	7	Frequency of urination	2
Dysuria	6	Fecal fistula	2
Abdominal mass	6	Postoperative fistula	2
Amenorrhea	5	Hemorrhoids	1
Menorrhagia	5	Malaise	1
Fever	5	Nosebleed	1
Dragging sensation	4	Draining umbilical sinus	1
Leukorrhea	3	Postoperative ventral hernia	1
Prolapsus	3	Indigestion	1
Constipation	3	Convulsions	1
General ill health	2	Urinary retention	1

sons. Certainly in a young person with evidence of ascites, tuberculous peritonitis should be considered as a strong possibility.

Weakness or susceptibility to fatigue, when persisting over a long period of time, should always arouse one's suspicions of a tuberculous condition, but this symptom was mentioned by only 13 patients among their chief complaints. The various types of fistulas or draining sinuses mentioned by 5 patients are symptoms which should also entail a careful search for a tuberculous process. The others listed in table 6 are either of no significance or will be considered later along with the general symptomatology.

Many symptoms not particularly stressed in the chief complaint were found on further questioning to be of more or less frequent occurrence. We have attempted to tabulate the symptoms as obtained

from the histories under four headings: (1) general symptoms, particularly those such as one should expect to find associated with a tuberculous condition; (2) digestive symptoms; (3) gynecological symptoms, and (4) urinary symptoms. Table 7 gives the relative frequency of various symptoms occurring under these headings.

From this table we again see the striking preponderance of pain as a symptom but draw no further diagnostic aid from it except as it can be linked up with more specific symptoms.

Fever and loss of weight are suggestive of a tuberculous condition, particularly if the fever is moderate and the temperature shows an afternoon rise. As has already been said, the presence of ascites in a young person is always suggestive of tuberculous peritonitis, and if this is associated with fever and loss of weight, the evidence becomes increasingly strong. A history of chronic cough or hemoptysis is important as a possible indication of pulmonary involvement. A history of pleurisy was obtained in 20, and there was definite pulmonary involvement in 40 of our cases.

TABLE 7.—*Symptomatology of Tuberculous Peritonitis*

1. General		2. Digestive		3. Gynecologic		4. Urinary	
Pain	169	Nausea and vomiting	51	Irregular or increased uterine bleeding	40	Dysuria	91
Fever	142	Nausea without vomiting	10	Amenorrhea, complete	40	Frequency	41
Loss of weight	115	Constipation	78	Scanty flow	26	Hematuria	6
Ascites	83	Diarrhea	13	Leukorrhea	122		
Cough	48	Constipation and diarrhea alternating	2	Dysmenorrhea	54		
Hemoptysis	11						

The digestive symptoms, again, are far from specific, and are such as may be found with a variety of intra-abdominal conditions. Kelly [20] stressed constipation as occurring in one half of his patients and stated that 20 per cent complained of pain on defecation. These symptoms are easily explainable on the basis of large pelvic masses exerting pressure on the rectum. Seventy-eight patients in our series were troubled with constipation. Diarrhea occurring alone, as in 13, or alternating with constipation, as in 2 of our cases, is more apt to occur when there is actual disease of the intestinal tract. Nausea and vomiting occur more frequently in those cases in which there is a widespread dissemination of the peritoneal process with extensive involvement of the upper part of the abdomen. In considering the digestive symptoms it must not be lost sight of that other diseases of the gastro-intestinal tract, such as ulcer, disease of the gallbladder, or appendicitis, may be present simultaneously with the tuberculous peritonitis, and although, as has been shown, varied and marked digestive symptoms may be produced by this disease alone, one should never fall into the error of assuming without proof that all of a patient's symptoms are due to a single morbid entity.

Menstrual disturbances of one kind or another aside from dysmenorrhea were noted in 106 cases. Forty of these patients had irregular or excessive uterine bleeding, which is of no great diagnostic aid since it is a symptom of so many different pelvic disorders. However, a complete amenorrhea in 40 patients and a scanty flow in 26 are more worthy of note. These should always lead one to look for tuberculosis, particularly tuberculosis of the genital organs, since they are symptoms which will result from a destructive process in either the ovaries or the endometrium, but on the other hand may also result from any wasting, debilitating, systemic disease. Leukorrhea occurred in 122 patients, but again this is a symptom common to many conditions. On the other hand, a profuse leukorrhea when associated with amenorrhea is suggestive.

Kelly [20] stated that pain on urination is the most characteristic of all the symptoms and found only 3 of 20 patients free from it. In our series not quite half the patients were troubled by this symptom, while only 41 complained of frequency. We have found no adequate explanation for the frequency of these symptoms, but it seems logical to assume that, in the adhesive variety of peritonitis adhesions between the bladder and other viscera might easily account for either one or both of them, while in the ascitic variety the pressure of abdominal fluid on the bladder would naturally lead to frequency. The presence of hematuria, which occurred in 6 of our cases, should always arouse a suspicion of renal tuberculosis, and in 2 of the 6 this lesion was actually demonstrated.

Owing to the diversity in the manifestations of the disease, clinical as well as pathologic, it is difficult to regard any single symptomatic syndrome as definitely characteristic. From our own experience, however, we believe that the presence of abdominal swelling and distention, particularly if there is definite ascites and a history of pleurisy, associated with abdominal pain or pelvic pain which is worse at the menstrual periods, with a low grade fever, higher toward evening, and loss of weight, with some digestive symptoms especially constipation, and with dysuria or frequency, or both, constitute a syndrome which should strongly arouse the clinician's suspicion of peritoneal tuberculosis. If in addition to these symptoms there is a menstrual disturbance, more particularly an amenorrhea or scanty flow combined with a profuse leukorrhea, the evidence becomes very strong.

Murphy [14] stressed the fact that in the serous ascitic variety of the disease alternate remissions and exacerbations of symptoms are frequently observed. He attributed the exacerbations to intermittent showers of tubercle bacilli thrown into the peritoneal cavity along with caseous material extruded from the patent fimbriated ends of the tubes.

This is a phenomenon well worth noting in observing the clinical course of these patients, and it has already been stated that 7 of our patients who gave a history suggestive of a chronic course were admitted during such an acute exacerbation.

Signs.—In addition to the subjective symptoms complained of by the patient, the observations on physical examination, particularly those referable to the abdomen and pelvis, were noted. On abdominal examination, tenderness was noted in 101, distention in 83, signs of free fluid in 53 and palpable masses in 42 patients. Pelvic examination revealed a variety of observations with various combinations. Table 8 gives a list of the various signs noted with their frequency.

It will be readily seen from the list in table 8 that there is nothing specifically to be made out from pelvic examination which can be considered characteristic of the disease. In rare cases tubercles were

TABLE 8.—*Observations from Pelvic Examination*

Bilateral indurated masses	59	Thickened vaginal wall	5
Pelvic adhesions and immobility	37	Tubercles or nodules felt per rectum	5
Pelvic tenderness	29	Tubercles palpable per vaginam	4
Unilateral indurated masses	25	Myomas	3
General pelvic induration	24	Thickened ureter*	1
Bulging masses in culdesac	19	Vaginal fecal fistula	1
Malposition of uterus	13	Tubercle-like nodules in cervix	1
Cystic masses	12	Rectal stricture	1
Relaxed vaginal outlet	12	Pelvic examination entirely negative	19
Indurated or thickened tubes	8		

* Years ago Leslie M. Sweetnam drew attention to the fact that a thickened ureter felt per vaginam almost invariably indicates a tuberculous kidney. (Personal communication from Dr. Thomas S. Cullen.)

actually palpated by rectum or by the vagina, but the percentage of cases in which this observation was noted is so small as to be of little significance. The other observations were all such as might belong to a great variety of pelvic conditions.

Pulmonary Tuberculosis.—On admission to the hospital, 59 patients were suffering from a more or less active pulmonary tuberculosis, or had a history of a recent pleurisy. Postoperative pleurisy was a complication of convalescence in 9 patients. An operation was performed on all patients in whom pulmonary activity was not sufficiently marked to make a short anesthesia unjustifiable. The final results in the cases that we have been able to follow up are tabulated later, with a note as to the presence or absence of active pulmonary disease.

The longer one works over the records of this group of patients with peritoneal and pelvic tuberculosis, the more does it seem likely that most of these patients may fairly definitely be considered as having had an original pulmonary focus from which all their trouble began, regardless of whether or not it was demonstrated during their stay in

the hospital. This is just an impression one gains from observing the frequency with which an anesthetic stirs up an acute pleurisy, and the greater frequency with which active or old pulmonary disease is demonstrated in the more recent cases, especially since the use of the roentgen ray as a diagnostic adjunct.

Tuberculosis Elsewhere.—Aside from the lungs, pleurae and peritoneal cavity, tuberculosis was found elsewhere in only a few cases. A definite tuberculous cervical adenitis was demonstrated in only 4 cases, though in a good many others there was a positive statement as to the enlargement of cervical glands, the nature of this enlargement, however, being uncertain. There was involvement of the kidneys in 2 cases, as shown at autopsy, after being diagnosed clinically by the presence of bacilli in the urine. In one of these a psoas abscess with involvement of the lumbar vertebrae was also found. In one case the autopsy showed a tuberculous otitis media and disseminated tubercles in the liver and spleen. Three patients died of either miliary tuberculosis or meningitis. Autopsies were obtained on all of these. One had a generalized miliary disease with meningeal involvement, another meningitis without the wide dissemination and the third a combination of the two. All of these patients except the 4 with adenitis, belong in the acute, desperately ill group.

Diagnosis.—The correct preoperative diagnosis was made and recorded in the history in 50 cases, or 27 per cent. In 115 instances the preoperative diagnosis was not specifically mentioned, but there can be little doubt from the description that the condition was recognized in many of these. In this group also are the cases in which tuberculosis was not recognized, but an operation was performed for myomata uteri, repair of a hernia, appendicitis, malpositions of the uterus, ovarian cysts and other conditions. A large percentage was apparently operated on for supposedly tuberculous salpingitis, when diseased tubes had been felt on pelvic examination, but there had been no clinical manifestations of the peritoneal dissemination. It is common for these patients to be in good physical condition, and this led to confusion in a few instances. In 14 patients the preoperative diagnosis was specifically stated as chronic salpingitis and the tuberculous nature was first discovered at operation.

The correct diagnosis in the 50 cases was made most frequently in the patients with ascites and abdominal tenderness and in whom a history of a recent pleurisy was obtainable, or pulmonary tuberculosis was demonstrable. In some of the cases with a history of bleeding tuberculosis was discovered in the endometrium, removed by curettage, and a laparotomy was later performed. In 2 instances tubercles were felt

on the peritoneal surfaces of the pelvis on rectal examination, and in 1 instance through a posterior colpotomy wound. In less advanced tubal cases the diagnosis was suggested occasionally from discrete nodules palpated along the course of the tubes. In advanced tubal cases the peculiar matted feeling of the pelvic viscera sometimes suggested tuberculosis.

The interpretation of the various abdominal tumors occurring in this series shows that in only 1 instance was there an elongated mass in the epigastrium interpreted as rolled up tuberculous omentum detected before operation—a condition so frequently mentioned in the literature. Localized accumulations of fluid were mistaken for ovarian cysts in 4 cases, and to explain the fixation in 1 case it was thought probable that the cyst was parovarian. One patient with much tenderness over the mass was thought to have a cyst with a twisted pedicle. Carcinoma of the ovary with abdominal metastases was the preoperative diagnosis in 3 of the patients past middle age.

Focus of Peritoneal Infection; Tuberculous Salpingitis.—In all but 9 of the 94 cases in which one or both tubes were removed tuberculosis was reported specifically in these structures. The clinical and gross pathologic diagnosis was certain in these 9, but a superimposed acute infection made the histologic diagnosis uncertain. Therefore, in 85 cases, or 45 per cent of the total series, tuberculosis of the tubes was proved to be present, and probably was the original focus in the peritoneal cavity. There were many interesting variations in this group. An occasional abdomen presented more active and more marked tuberculosis in the upper portion with small closed off tubes, which on section showed a chronic process, suggesting that the pelvic process was healed or in process of healing, while activity was still continuing in the upper part of the abdomen. In one of these a diverticulum of the large bowel was present in an area much affected, and suspicion was directed to this as a focus. On section, however the tubes showed a chronic tuberculous process. Similar cases were those with the appendix much involved but also with tuberculous tubes.

In at least 3 cases large tuberculous peritoneal cysts were described with the open fimbriated extremities of one or both tubes opening into them.

There are two groups of cases in which it seems impossible to tell whether the tubes are the original pelvic focus or not. One group includes those patients with an advanced and severe peritoneal process in whom the tubes could not be seen during operation, and in whom all pelvic structures were diseased. The other is the disseminated ascitic type of case in which the patients have a uniform distribution of

tubercles over the abdomen, or perhaps a more prominent distribution in the upper part of abdomen, and in whom the tubes were not removed. As will be seen, there were a few, 6 to be exact, of the latter group in which an exploratory laparotomy was first done and symptomatic tubal disease developed later, requiring a second operation. It is certain, however, that this does not always happen.

Tuberculosis of the Endometrium.—In 66 instances the endometrium was available for examination, either because a diagnostic curettage was done for bleeding or because the uterus was removed. Thirty-seven of these showed a tuberculous involvement of the tissue. The association with symptomatic uterine disorders in the 37 cases was as follows: leukorrhea, 24; amenorrhea, 20; metrorrhagia, 2; menorrhagia, 7, while in 8 of the patients the periods had been normal.

It is thus seen that leukorrhea is most commonly associated with tuberculosis of the endometrium. Amenorrhea also occurs frequently but it would seem unwise to attribute its presence to the endometrial disease alone, for 5 of these patients had advanced pulmonary tuberculosis, and several had marked involvement of both ovaries with probable destruction of their function. Infantilism of the genital organs, which is often stated in the literature as frequently associated with tuberculosis of these organs, was noted only once in this series.

In the entire series, 22 of 68 patients with clinically active pulmonary, bone or urinary tuberculosis had had amenorrhea. As a rule, this symptom accompanied the more advanced cases, and was often met with in patients who could not be operated on because of the extent of the pulmonary process. We have proof in only 5 of these that the endometrium was tuberculous.

Pathologic Types.—In 1903, Murphy [14] divided the lesions of tuberculous peritonitis into four groups on a pathologic basis as follows:

I. The Disseminated, Exudative, Miliary, Nonconfluent Serous (Ascitic) Variety: The tubes in this group are usually patent and caseous material may be expressed from their lumina. The pelvic peritoneum bears the brunt of the infection, but the whole peritoneal cavity may be involved. Ascitic fluid, clear yellow, slightly sanguineous, or a little cloudy, from a few ounces to large quantities, may be present.

II. The Nodular Ulcerative or Perforative Variety, the Least Common Type: In this variety, the whole force of the destructive process is concentrated into small areas, and in these areas not only the peritoneal coat but the deeper structures, as the intestinal wall, the mesentery, uterus or ovaries, are destroyed or changed into caseous masses surrounded by dense connective tissue barriers or adhesions. The tubes are usually closed or fixed at their fimbriated ends to the adjacent viscera.

III. The Adhesive, Fibroplastic, Cystic, Partition or Obliterative Variety: In many cases this group represents the healing stages of the disseminated ascitic variety, but it has been pointed out that these adhesive varieties sometimes arise without previous ascites. In this group occur the bizarre tumors of localized accumulations of fluid, rolled up omentum, etc. The tubes are closed with adnexal masses often present. Fresh adhesions are fibrinous in character; the older cases present very tough fibrous bands uniting contiguous structures.

IV. Tuberculous Peritonitis with Mixed Infection: A secondary infection may be superadded to cases belonging to any of the preceding types. The colon bacillus is a common invader, and a localized or a fairly general peritoneal infection may occur. This group of patients presents the most severe and even desperate form of the disease, death frequently occurring as an immediate result of the secondary infection. If surgical drainage is instituted promptly, some may live, but fistulas frequently follow the necessary use of drains.

Three of the groups described by Murphy (groups I, III and IV) are common and seem to us useful in helping to visualize the processes that take place within the abdomen, and in understanding the various manifestations of the disease. We have found classification of our cases according to this scheme practical in a large proportion of them, but when for want of adequate description in the hospital record, or because the abdomen was not opened or could not be thoroughly explored, the group is in doubt, we have omitted such cases (25 in our series) from the classification.

We have tabulated 42 cases as fairly clearly belonging to Murphy's group I, but it must be made plain that, although in the hospital histories explicit notes were not made in all cases as to the patency of the tubes, no large masses were found in the pelvis. Classification was possible in such cases on the basis of general dissemination of tubercles and the presence of ascites. We have frequently an overlapping of the simple ascitic cases (group I) with those of group III, in which pelvic masses have formed and the abdomen is being obliterated or partitioned off by adhesions. In fully half a dozen cases this change was nicely exemplified at operations a few months or a year or so apart, a case which had appeared as belonging to the simple ascitic variety at the first operation presenting the features of an adhesive or cystic partition variety at the second.

None of the patients with the simple ascitic variety died in the hospital. There did not seem to be a tendency for the fluid to reaccumulate to an extent sufficient to make further surgical procedures imperative. Of the 42 patients, 5 died of pulmonary tuberculosis within five years after leaving the hospital. Twenty are living and well, and

the remaining 17 could not be traced. The operation most frequently performed in this group was a simple exploratory laparotomy with evacuation of the ascites and removal of a bit of tissue for pathologic confirmation of the clinical diagnosis.

We have put none of our cases in Murphy's group II, because we could never feel sure that any of them coincided with his idea of the nodular ulcerative variety. However, we think that if some of the severe generally disseminated cases that we have placed in groups III and IV could have been seen at an earlier stage, they probably would have fallen into this group.

To group III, the fibroplastic variety, we have assigned 108 cases. The most frequent type in this group was found to be that in which there were adnexal masses and a dissemination of tubercles. In a few there was generalized ascites and in many there were localized accumulations of fluid. The most characteristic observation was wide-spread

TABLE 9.—*Treatment of 187 Patients with Tuberculous Peritonitis*

Operation	Number	Previous Operations	Died in Hospital	Subsequent Operations	Living After Discharge	Died After Discharge	Untraced
No operation	17	0	5	0	2	2	8
Posterior colpotomy	12	1	5	11	3	0	4
For fistulas	6	6	2	0	3	0	1
Exploratory laparotomy	74	6	11	8	15	3	44
Operations, conservative	28	5	1	3	8	4	15
Complete pelvic operation	66	7	5	3	20	8	33

abdominal adhesions. In general these were cases of longer standing than those in group I, and the clinical course was more apt to be of a chronic, sometimes even of a latent, nature. The operation most frequently performed was removal of the diseased pelvic structures when possible; otherwise an exploratory laparotomy with evacuation of the cystic accumulations of the fluid was carried out.

Six of the patients belonging to this group died in the hospital, 1 of shock, 2 of intestinal obstruction, 1 of acute secondary peritonitis, 1 of generalized tuberculosis and 1 of pulmonary embolus. We have been able to trace 21 patients from this group who are still living. In most of these the pelvic focus was entirely removed, but 1 is living after thirty-five years in whom the pelvic masses were so extensive that it seemed unwise to attempt to remove them.

We have 12 cases in the secondarily infected group (IV). The patients were all desperately ill, and operation was undertaken only as a last resort. They all died in the hospital either as an immediate result of the preexisting infection or from fistula formation and inanition following surgical drainage.

It must again be repeated that because of overlapping of disease types, confusion in the records and other reasons these figures are all only approximations.

Treatment.—The treatment of 187 patients with tuberculous peritonitis is given in table 9. All but 17 of these women were operated on. For 170 patients, we have 185 operations. The table represents operations, not patients.

No Operation: Seventeen patients were not operated on. The diagnosis of tuberculous peritonitis in these, however, seems clear because of the combination of unmistakable signs of pulmonary and abdominal tuberculosis. All but 2 had advanced pulmonary tuberculosis or acute pleurisy and were transferred to the medical service of the hospital or to sanatoriums for treatment. The remaining 2 had advanced renal tuberculosis at the time of their admission or previously. Five died in the hospital, 3 of advanced pulmonary and generalized tuberculosis, 1 of hemorrhage from the intestinal tract and 1 of advanced renal tuberculosis.

Twelve left the hospital. Only 2 are known to be living today. One (eight years after discharge) is in good health so far as we can ascertain. Another is living after three years, practically all spent in a sanatorium, but is not well, although the abdominal symptoms have disappeared, and there are no masses palpable on pelvic examination. We know that 2 died from advanced pulmonary tuberculosis within a year after leaving the hospital. Eight could not be traced.

Posterior Colpotomy: This operation was performed one or more times on 12 patients for accumulations of fluid or pus in the culdesac. All of these patients except 1 were submitted to an abdominal operation. Section had been performed six months and nine years previously in 2 cases, was performed at the time of the posterior colpotomy in another, the remainder following posterior colpotomy from one month to a year. In the patient who did not come to abdominal section, the diagnosis was made from the shotlike tubercles palpable over the peritoneal surfaces in the pelvis at the time of the posterior vaginal puncture.

Five died in the hospital following abdominal section. Four died of fistula formation and inanition. One died of a colon peritonitis. Simple exploratory laparotomy and drainage were done in 4 of those who died. In the other both tubes were removed.

Seven left the hospital. Of these, 4 had undergone a complete operation. In 2 an exploratory laparotomy had been performed. In 1 case no secondary operation was done. Three are living and well after complete operations. Four cannot be traced.

Closure of Fistulas: Four patients with tuberculous peritonitis were operated on for chronic fecal or urinary fistulas, having previously had 1 or more operations elsewhere. Two were cured, 1 was improved and 1 died after a resection of a portion of the terminal ileum.

After abdominal drainage for secondary infection, two patients developed fistulas. In closing one of these it was necessary to resect the cecum. Both patients died.

Exploratory Laparotomy: Simple exploratory laparotomy with excision of tissue was performed 73 times for one or more of the following reasons: (1) for drainage in desperately ill, secondarily infected patients, or to evacuate an ascites; (2) when removal of large pelvic masses seemed hazardous; (3) when the tubes looked patent and it was wished to preserve the child-bearing function if possible; (4) by choice—to prove the therapeutic result of simply opening the abdomen.

Six of these patients had undergone a posterior colpotomy one or more times before the abdomen was opened. The punctures were done for pelvic accumulations of pus in 4 cases, in all of which the outcome was eventually fatal. Two were done for accumulations of clear fluid in the culdesac.

Drainage was employed in 25 cases. Eight of the patients were desperately ill from secondary infections. In 17 there was no obvious secondary infection. In the 25 are included the earlier cases of the hospital when drainage was employed as a routine measure. Sufficient commentary on the question of drainage is supplied by the fact that at the present time drains are never employed in tuberculous cases except when necessary for secondary infection or to control bleeding. When drains are used, the immediate postoperative course is apt to be more difficult; incisions break down oftener with danger of hernia or fistulas develop. Thirteen of the 25 cases, in which drains were used, were complicated. In 6, draining sinuses persisted for a long time. The remaining 12 seem to have been uncomplicated as far as can be gathered from the hospital records.

Eleven of these 73 patients died in the hospital. Eight were desperately ill when admitted, suffering from the secondarily infected variety of the disease, and died of infection or of fistula formation and inanition. One died of shock, 1 of intestinal obstruction and another of peritonitis following accidental perforation of the adherent small bowel during the posterior colpotomy.

The remaining 62 left the hospital well or improved. Seven are known to have undergone subsequent operations. Five did not get well until the tubes were removed. One of these had no trouble for eight

years, but finally underwent a salpingectomy nine years after the exploratory laparotomy. In 4 of the 5 the tubes looked normal at the time of the original operation, but were considerably involved at the time of removal. One patient was submitted to a complete operation two years after the exploratory laparotomy. In 1 case two pelvic punctures were performed within six months after the exploratory laparotomy.

Four of the patients who left the hospital are dead. Two died of pulmonary tuberculosis within two years. One died of intestinal obstruction twenty-seven years after operation. The cause of death in the fourth, nineteen years after operation, is unknown.

Fifteen are living and well from eighteen months to thirty-five years after operation. In only 3 of these was gross tubal involvement found at the time of operation. In the others the disease was of the discrete disseminated variety with patent tubes and ascites. None have become pregnant.

Forty-three could not be traced.

Conservative Surgical Intervention: Twenty-eight patients were submitted to various forms of conservative pelvic surgical intervention. Both tubes were removed in all except 6 cases in which one tube was left or plastic work was performed. The tubes were removed following exploratory laparotomy in 4 cases. They had appeared normal at the original operation and were not thought to be the focus of the tuberculous infection. Drainage was employed in 5. Two of these are recorded as acquiring persistent sinuses. The other 3, in 2 of which pelvic drains were used, suffered from no complications.

One of the 28 died in the hospital, a patient with a severe secondary infection, on whom a laparotomy was performed following posterior colpotomy. Twenty-seven left the hospital. Three were operated on again later. Two underwent complete operations because of continued severe pain. The third had painful adhesions which were released. A fourth, six months after plastic work on the tubes, had been advised to have another operation because of persistent symptoms.

Four of the 27 are dead. One died of pulmonary tuberculosis within a year. Another died of pulmonary embolus following cholecystectomy four years after salpingectomy. The cause of death in the other 2 is unknown—nine and two years after operation. Seven are living and well from 1 to 30 years after operation. Fifteen cannot be traced.

Complete Operation: Both tubes and ovaries were removed in 66 cases. These represent, as a rule, the severer forms of the disease, for ovaries were saved whenever possible. In all but a few of these patients the uterus was also removed. Panhysterectomy was performed 10 times, supravaginal hysterectomy, 51 times.

Four operations with removal of all the internal generative organs followed one or more posterior colpotomies. So far as we can ascertain, the complete operation was done after previous conservative surgical intervention in only 2 cases—both for continued severe dysmenorrhea—and in only 1 case following an exploratory laparotomy.

Drainage was employed in 34 of these operations. Pelvic drains were employed in 25 cases and abdominal drains alone or combined with the pelvic drains in 12 cases. Wound infection, sinuses or fistulas occurred in 8 cases. A high postoperative fever was also noted in some. In the 32 cases in which drainage was not performed, wound infection, sinuses or fistulas are recorded only four times. Of course, it was only in the worse cases that drainage was instituted, in some after accidental injury to the rectum. Five of these patients died in the hospital, the causes being: generalized tuberculosis, 2; pulmonary embolus, 1; secondary peritonitis in a diabetic patient, 1, and intestinal obstruction, 1.

Sixty-one left the hospital well or improved. In 2 a second laparotomy was done later for release of adhesions. In 1 case a posterior colpotomy was performed later for an accumulation of fluid in the pelvis.

We know that 8 died from 1 month to five years after operation, and in 4 cases we have definite knowledge that the death was due to pulmonary tuberculosis. Twenty are alive and well from a few months to thirty-four years after operation. Thirty-three cannot be traced.

RESULTS

Before beginning a tabulation of the results, a brief comment may be made on the difficulties that we have encountered in tracing the subsequent course of the patients after their discharge from the hospital. It will be seen by reference to table 9 that 104 of the 187 patients are untraced, but when we consider that our statistics extend over a period of thirty-eight years and that 90 of our patients were negroes and many of the whites were from among the foreign element, the difficulties in tracing them become obvious. This part of the work has been diligently pursued over a period of more than two years, and every available means has been employed to trace the patients, so that the failure to find 104 of them is rather disappointing. Letters were first sent to every possible address obtained from the ward and dispensary records of the patients. After these letters had been returned, an attempt was made personally to seek out the patients who had given Baltimore addresses. This method was effective in collecting data on a few additional cases, but in many it was found that the district had been absorbed by industrial expansion. In other cases, addresses were

TABLE 10.—*Type of Disease and Operation and Cause of Death in Twenty-Six Patients*

Number	Pulmonary Activity	Days in Hospital	Type of Peritoneal Disease	Operation	Cause of Death
U-12537	No	10	Disseminated; secondary infection	Exploratory laparotomy; closure of tuberculous perforation	Secondary infection
U-9911	No	65	Disseminated; secondary infection	Exploratory laparotomy; closure of fistula	Fecal fistula and inanition
U-8712	No	55	Disseminated; secondary infection	Posterior colpotomy; exploratory laparotomy	Fecal fistula and inanition
30544	No	63	Disseminated; secondary infection	Posterior colpotomy; exploratory laparotomy	Fecal fistula and inanition
27976	No	47	Adhesive	Complete pelvic operation	Diabetes; localized infection
27504	Yes	32	Localized secondary infection	Drainage of abscess; resection of cecum	Fecal fistula; generalized tuberculosis
26055	Yes	40	Disseminated; secondary infection	Posterior colpotomy; conservative pelvic	Infection and miliary tuberculosis
25345	No	1	Chronic adhesive	Exploratory laparotomy	Shock
24669	No	6	Disseminated; pelvic masses	Complete pelvic	Pulmonary embolus
22964	No	23	Chronic adhesive	Complete pelvic	Generalized tuberculosis
21769	Yes	2	Disseminated; pelvic abscess	Exploratory laparotomy	Secondary infection
18887	No	43	Disseminated; secondary infection	Posterior colpotomy; exploratory laparotomy	Fecal fistula and inanition
17589	Yes	19	Chronic adhesive	Complete pelvic; enterostomy	Intestinal obstruction
17261	Yes	14	Disseminated; pelvic masses	Complete pelvic	Pulmonary tuberculosis ?
15499	Yes	1	Generalized	None	Generalized tuberculosis
14067	?	7	Disseminated; secondary infection	Exploratory laparotomy	Secondary infection
13023	No	69	Disseminated; pelvic abscess	Exploratory laparotomy; curettage of fistula	Fecal fistula and inanition
12908	No	4	Disseminated; secondary infection	Exploratory laparotomy; colostomy	Secondary infection; general tuberculosis
10805	Yes	6	Disseminated	None	Generalized miliary tuberculosis
9966	No	97	Disseminated; secondary infection	Left nephrectomy	Uremia; generalized tuberculosis
6884	No	5	Adhesive; secondary infection	Complete pelvic	Secondary infection
6209	Yes	16	Intestinal ulcers; generalized	None	Intestinal hemorrhage
5240	No	18	Generalized; pelvic abscess	Posterior colpotomy; exploratory laparotomy	Secondary infection
4165½	?	26	Disseminated; secondary	None	Psoas abscess; generalized tuberculosis
1358	?	30	Chronic adhesive	Complete pelvic; release of adhesions	Intestinal obstruction
846	Yes	7	Disseminated	None	Generalized tuberculosis

found to be those of boarding houses at which out-of-town patients were staying when admitted to the hospital. This method is often adopted by certain colored patients from other states in an attempt to secure free admission. We feel, therefore, that though the results obtained are disappointing, the facts that we have been able to collect are probably from the more intelligent of the series and therefore probably of as much value as from a larger group.

Died in the Hospital.—Twenty-six patients died in the hospital. Five of these were not operated on. The operative mortality rate is then 11.3 per cent. The major causes of death in the patients operated on are as follows: (1) fecal fistula and inanition with slow down hill postoperative course, 5; (2) heavy secondary peritoneal infection with shorter postoperative course, 7; (3) generalized tuberculosis, 4; (4) intestinal obstruction, 2; (5) primary renal tuberculosis, uremia, 1; (6) shock, 1, and (7) pulmonary embolus, 1.

TABLE 11.—*Types of Operations and Absence of Pulmonary Activity in the Two Groups*

	Living After Leaving Hospital, 47	Died After Leaving Hospital, 18
Exploratory laparotomy	15	5
Complete pelvic operation	20	7
No operation	2	2
Other operations	10	4
Pulmonary activity	10	10
Lungs clear	35	7
Questionable activity	2	1

It is realized that the first three causes of death overlap to a great extent, particularly in that in many of the patients with a secondarily infected type drainage was instituted judiciously with immediate improvement, the patients dying later of fistula formation and inanition.

The five patients not operated on died of: (1) generalized tuberculosis, 3; (2) intestinal hemorrhage, 1; (3) primary renal and generalized tuberculosis, 1.

Table 10 shows the type of disease, type of operation and cause of death in the 26 patients who died in the hospital.

We have succeeded in tracing 65 of 161 patients discharged from the hospital. Eighteen of these died in from one month to twenty-seven years after leaving the hospital. Most of the deaths were from pulmonary tuberculosis within the first five years after discharge. The patient who lived for twenty-seven years died of intestinal obstruction. The patients who died of pulmonary tuberculosis within the first year after discharge were, as a rule, those who had showed activity of the pulmonary process while in the hospital.

TABLE 12.—*Individual Results in Patients Still Living*

Number	Pulmonary Activity	Type of Peritoneal Disease	Operation	Well After
U-4880	No	Chronic adhesive; fistula	For cure of fistula	3 months
U-2824	No	Encapsulated ascites	Posterior colpotomy; complete pelvic	2 months
U-2743	Yes	Disseminated, ascites; pelvic masses, adhesions	Exploratory laparotomy; complete pelvic	2 years
U-1050	No	Encapsulated ascites	Exploratory laparotomy	1½ years
M-41744	Yes	Ascites	None	8 years
30037	Yes	Disseminated; ascites	Exploratory laparotomy	2 years
30091	No	Pelvic masses	Complete pelvic	3 years
30029	Yes	Disseminated	Complete pelvic	1 year
29951	No	Pelvic masses; encapsulated; ascites	Complete pelvic	1 year
29193	Yes	Healing; adhesive	For cure of fistula	4 years
28863	Yes	Disseminated; ascites	None	Not well 3 years
28657	No	Disseminated; ascites	Exploratory laparotomy	4 years
28449	No	Adhesive, chronic	Conservative pelvic	3 years
28032	Yes	Adhesive, chronic	Complete pelvic	6 years
28029	No	Disseminated; ascites	Exploratory laparotomy	5 years
27715	Yes	Pelvic masses; chronic adhesive	Complete pelvic	5 years
25564	No	Disseminated	Exploratory laparotomy	7 years
24949	No	Encapsulated fluid; adhesive	Posterior colpotomy; complete pelvic	7 years
24495	No	Disseminated; ascites; adnexal masses	Exploratory laparotomy; conservative pelvic	9 yr., 3 mo.
24122	No	Disseminated; ascites	Exploratory laparotomy	9 years
23874	No	Disseminated; ascites	Exploratory laparotomy; partial salpingectomy	9 years
23729	No	Disseminated; ascites	Complete pelvic	1 year
22098	No	Pelvic abscess; large pelvic masses	Posterior colpotomy; complete pelvic	12 years
21971	No	Disseminated; ascites	Exploraory laparotomy	11 years
21933	No	Disseminated	Complete pelvic	12 years
18367	No	Disseminated; ascites	Exploratory laparotomy	13 years
19320	No	Disseminated; ascites	Exploratory laparotomy	14 years
19176	Yes	Encapsulated; ascites	Conservative pelvic	14 years
17447	No	Tubes closed; localized	Plastic on uterine cornua	Not well 6 months
15161	No	Disseminated; large pelvic masses	Complete pelvic	19 years
14400	Yes	Chronic adhesive	Complete pelvic	1 year
12473	?	Disseminated; ascites	Exploratory laparotomy	3 years
10437	No	Encapsulated fluid	Exploratory laparotomy	24 years
9849	No	Disseminated; ascites	Exploratory laparotomy	25 years
9735	No	Pelvic masses; pus in pelvis	Complete pelvic	2 years
8596	No	Pelvic masses; ascites	Complete pelvic	23 years
8579	No	Disseminated; ascites	Conservative pelvic; complete pelvic	28 years
7645	?	Disseminated; ascites	Exploratory laparotomy	28 years
7698	No	Disseminated; ascites	Right salpingectomy	27 years
6547	No	Disseminated	Conservative pelvic	30 years
6527	No	Disseminated; ascites	Complete pelvic	30 years
6327	No	Adhesive	Complete pelvic	29 years
5098	No	Disseminated; ascites	Conservative pelvic	30 years
4868	No	Disseminated; ascites	Exploratory laparotomy	31 years
3303	?	Masses in pelvis	Complete pelvic	32 years
2637	No	Disseminated	Complete pelvic	34 years
2045	No	Ascites; pelvic masses; not operable	Exploratory laparotomy	35 years

Forty-seven are living, and it is a fact worth noting that these patients almost uniformly report themselves as very well, no matter what the operation or type of disease. There have been no pregnancies in any of the patients whom we have been able to follow up.

The types of operations performed and the presence or absence of pulmonary activity in these two groups are summarized in table 11.

It will be seen from table 11 that 11 of the 18 patients who have died since leaving the hospital had definite or questionable pulmonary

TABLE 13.—*Individual Results in Patients Who Died After Leaving Hospital*

Number	Pulmonary Activity	Type of Peritoneal Disease	Operation	Cause of Death	After Discharge
20908	No	Disseminated; ascites; upper part of abdomen	Exploratory laparotomy	Pulmonary tuberculosis	1 yr.
28806	Yes	Masses in pelvis; ascites	None	General tuberculosis	1 day
28797	Yes; lung and spine	Ascites	None	General tuberculosis	1 yr.
26515	Yes	Fresh adhesive	Exploratory laparotomy	Pulmonary tuberculosis	1 yr.
26232	No	Chronic adhesive	Conservative pelvic	?	2 yrs.
26209	No	Disseminated; ascites	Complete pelvic	?	1 mo.
20833	Yes	Chronic adhesive; enlarged glands	Complete pelvic	?	?
24196	No	Disseminated; ascites	Exploratory laparotomy	?	4 yrs.
21258	No	Chronic adhesive	Conservative pelvic	?	9 yrs.
18287	Yes	Disseminated ascitic; pelvic masses	Exploratory laparotomy; complete pelvic	Pulmonary tuberculosis	4 yrs.
14872	Yes	Pelvic masses; fistula to bowel	Complete pelvic	?	?
13616	?	Fresh adhesive	Exploratory laparotomy	?	19 yrs.
10992	Yes	Fresh adhesive	Complete pelvic	?	?
9550	Yes	Disseminated; ascites	Conservative pelvic	Pulmonary tuberculosis	4 yrs.
8809	Yes	Disseminated	Complete pelvic	?	?
6506	No	Disseminated; ascites	Left salpingectomy	Embolus after cholecystostomy	4 yrs.
3907	No	Disseminated; ascites; upper part of abdomen	Exploratory laparotomy	Intestinal obstruction	27 yrs.
1739	Yes	Disseminated	Complete pelvic	Pulmonary tuberculosis	1 yr.

activity during their stay in the hospital, while only 12 of the 47 who are still living showed such activity.

Tables 12 and 13 present the individual results in these two groups of cases, showing at the same time the type of disease, the type of operation and the presence or absence of pulmonary activity.

CONCLUSIONS

In thus reviewing the statistical data of 187 patients with tuberculous peritonitis treated on the Gynecological Service of the John Hopkins Hospital, we have been able to reach the following conclusions:

1. The incidence has been small as compared with other statistics gathered from the literature.

2. The incidence has been more than twice as great among colored as among white patients.

3. There has been a decided decline in incidence during the period under consideration, from 1889 to 1927. This has been more uniform and striking in the white than in the colored race.

4. The disease is most common among young adults in the second, third and fourth decades of life.

5. There is no striking etiologic relationship between pregnancy and tuberculous peritonitis to be derived from our series.

6. The disease may present all possible variations in the severity of its clinical manifestations but in the majority of cases it runs a chronic course.

7. Pain is the most constant of all symptoms, ascites the most suggestive of all signs.

8. Active pulmonary tuberculosis is frequently present before or after an anesthetic in tuberculous peritonitis (39 per cent). Healed lesions of some extent are found particularly frequently since the advent of the roentgen ray as a diagnostic adjunct.

9. Active pulmonary involvement while in the hospital seriously affects the prognosis during the first five years after operation.

10. All of the tubes removed from patients with tuberculous peritonitis showed tuberculosis of the endosalpinx. Individual records support the contention that in the adult female the tubes are usually the primary abdominal focus of the peritoneal disease.

11. Tuberculosis of the endometrium occurred in about half of the cases in which it was examined, but these as a rule were cases in which the disease was very extensive. Leukorrhea and amenorrhea are frequently associated with involvement of the endometrium, but other causes such as extensive pulmonary disease or destruction of the ovaries are often present to account for the amenorrhea.

12. In the ascitic disseminated type of tuberculous peritonitis the patient is usually treated by exploratory laparotomy with evacuation of the fluid. Patients with this type of the disease usually die only of pulmonary involvement. With treatment in a good sanatorium, the prognosis is excellent.

13. Patients with the adhesive cystic variety and pelvic masses are treated by removal of the diseased adnexae if possible; if not, by exploratory laparotomy. The prognosis is good if the tubes are completely extirpated. Pulmonary tuberculosis is the menace in the cases of shorter duration.

14. In the secondarily infected group, the patients are desperately ill. Surgical drainage is necessary to prolong life, but is undertaken only as a last resort. Death follows later from fistulas with resulting inanition, pulmonary tuberculosis not being a factor. Secondary

infection occurs usually only in those suffering from a very old, advanced peritoneal tuberculosis, and who would probably have already succumbed had there been much pulmonary activity.

15. With the modern methods of anesthesia available, ethylene anesthesia should be employed in preference to ether, since pulmonary involvement has been shown to be a frequent factor.

16. Operation should be followed by prolonged care in a sanatorium whenever possible.

A REVIEW OF UROLOGIC SURGERY

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(Concluded from p. 542)

PROSTATE GLAND

Hypertrophy.—Cammidge [39] stated that diabetes is particularly likely to develop during middle life. In a consecutive series of 850 cases, 495 patients (58 per cent) were aged 41 years or more when sugar was discovered in the urine. Although hypertrophy of the prostate gland is a later manifestation of senescence than diabetes, the approximation of the age of maximal onset makes it likely that one may be a complication of the other.

Many operations may be performed on patients with diabetes with no more than average risk, provided careful and proper preoperative and postoperative treatment is given. In order to prevent diabetic coma, it is necessary to eliminate from the body, as completely as possible, the source of the intermediate toxic products of metabolism giving rise to the condition, to increase the power of the tissues to store and utilize carbohydrate to a maximal extent, and to supply easily digested and absorbed carbohydrate in sufficient quantity for the needs of the organism. The first requirement may be met by limiting the intake of protein and reducing the fat of the diet to a minimum. The second requirement is partially fulfilled at the same time, for an excess of fat interferes with the storage and utilization of carbohydrate, as well as being a potential source of toxic derivatives in diabetic patients. There is rarely sufficient improvement in carbohydrate storage and utilization brought about by dieting alone so that surgical treatment can be carried out, and it is best to increase the patient's own powers artificially by giving insulin, for a short period at least, before and after the

39. Cammidge, P. J.: Prostatectomy in Diabetics, Brit. J. Urol. **1**:258, 1929.

operation. With the help of insulin, it is possible to increase the storage capacity to any desired extent, and, if necessary, the whole of the energy requirements of the body can also be supplied temporarily by dextrose.

Because many elderly diabetic patients are unusually fat, particular care must be taken in preparing them for operation. A more prolonged period of careful dieting is required in order that the surplus fat may be removed and the weight may be reduced to at least the average level and preferably a little below. The preparation of the patient with advanced diabetes, whose powers of carbohydrate, fat and protein metabolism are seriously deficient, presents another difficult problem. The patient must be regarded primarily as diabetic, and surgical procedures should not be undertaken until metabolic defects are thoroughly under control. Usually two or three months' treatment with diet and insulin are required. If he responds as he should to this treatment, there is a possibility that when the prostatectomy has been carried out successfully further improvement in metabolism may follow. In one of Cammidge's cases the urine was kept sugar-free only by two daily doses of insulin of 20 units before the operation, but afterward it was found possible to reduce the dose gradually, and eventually the urine remained free from sugar, and the blood sugar ranged within normal limits, on the same diet without any insulin.

There should be as brief a period of anesthesia as possible for operations on diabetic patients, and a two-stage operation, with an interval between for recovery, is usually better than prostatectomy carried out at one time. All anesthetics appear to diminish the alkalinity of the blood and to increase the sugar content, but there is a considerable difference in the extent of the changes produced by various anesthetics. Chloroform is the most dangerous and should not be administered to such patients under any circumstances; ether is less harmful, but gas and oxygen or spinal anesthesia is best.

A diet free from fat should be the invariable rule for at least three or four days after the operation. When this dangerous period has been safely passed, greater variance may be permitted gradually, although in the two-stage operation the amount of fat allowed in the interval should be strictly limited. Carbohydrate, including the allowance of dextrose and fruit juice, should constitute the bulk of the diet, and sufficient insulin should be given to maintain the blood sugar as nearly as possible within the normal range. Acidosis discovered at an early stage can usually be controlled by making suitable alterations in the diet and cautiously administering alkalis by mouth. It is generally better to commence the treatment with an intravenous injection of about 1 liter of warm, 10 per cent solution of dextrose, given at a rate not exceeding from 200 to 300 cc. each hour, with 10 units of insulin sub-

cutaneously at once and at hourly intervals afterward until from 30 to 40 units have been administered.

Devoting a few days or weeks to the preparation of a diabetic patient may ultimately make the difference between success and failure of the operation.

Harris[40] has successfully performed his operation of complete closure, without mortality, in 84 of 92 consecutive prostatectomies for benign prostatic hypertrophy, during a period of eighteen months.

Harris used the following operative technic: A transverse incision, from 5 to 7.5 cm. long, is made through the skin and fat 2.5 cm. above the top of the symphysis pubis, or about 3.5 cm. above, if only preliminary cystotomy is intended. The bladder is picked up with tissue forceps and opened, and the peritoneum is reflected to its topmost part. The intra-urethral method of bimanual enucleation of the prostate gland is carried out and the gland is removed. Electrically-lighted bladder retractors are then inserted.

For reformation of the floor of the prostatic urethra a triangular flap of trigonal tissue is drawn down into the prostatic cavity and sutured to the posterior portion of the floor of the cavity as close as possible to, and often picking up, the torn edge of the prostatic urethra. A long pair of angular ring forceps is passed into the prostatic cavity to pick up the capsule at a point low on the posterior wall. With slight traction this is easily brought into view in most cases. A special needle is then passed deeply from above downward by means of a special needle holder; this enters the mucosa from 0.83 to 1.25 cm. behind the prostatic rim and emerges deep in the prostatic cavity, having either passed deeply to or transfixed the tissue previously caught up by the ring forceps. The needle is then rotated upward by compression of the handle of the holder and emerges from the prostatic cavity into the bladder, where a loop of catgut is placed in its slot by a special carrier. The spring is released and the needle retraces its track armed with the catgut. When this is tied, a tongue-shaped flap of trigone is drawn down into the cavity, the horizontal trigonal shelf being converted into a more or less vertical gutter.

For obliteration of the prostatic cavity two or three anterior transverse sutures of catgut are used, traversing the prostatic cavity deeply from side to side. The first stitch passes deeply in the plane of a tangent to the foremost part of the prostatic ring, penetrating the mucosa well out on each side, taking as large a bite as the needle will hold and just skimming the floor of the prostatic cavity in the depths. This stitch is drawn tight and tied, and its ends held taut while the

40. Harris, S. H.: Suprapubic Prostatectomy with Closure, Brit. J. Urol. **1**:285, 1929.

second stitch is passed parallel to the first and about 1 cm. farther back. A rubber catheter is then passed through the urethra into the bladder. The tip of the catheter is drawn up out of the bladder and its eye transfixed by a needle armed with a length of silkworm gut. This is used to tether the catheter to a glass rod laid along the front of the abdominal incision.

To close the incision in the bladder one suture only of number 3 plain catgut is generally used. It is of an extended figure-8 type with three loops. The needle first penetrates the aponeurosis and rectus muscle at the lower angle of the wound on the left side, crosses over to the opposite side and picks up a good bite of the muscle of the bladder about 2 cm. external to the incision in the bladder. It then crosses back to the left side, and, returning to the right, picks up the edges of the incision, either just missing or just picking up the mucosa. It is then again carried back and picks up the muscle of the bladder on the left side about 2 cm. external to the incision. Finally, it crosses again to the right and penetrates the rectus muscle and aponeurosis from within outward. When this suture is drawn tight the cut edges of the incision of the bladder are brought into close apposition and inverted 2 cm. into the bladder, the muscular wall of which is fixed snugly to the abdominal parietes, so that the space of Retzius is obliterated and dead spaces are not left.

Convalescence is simple and the patient suffers little disturbance. Irrigation of the bladder is not practiced, only enough fluid being injected, when necessary, to free the catheter of clots. The catheter is retained in position until the tenth day. Usually there is no leakage of urine through the wound during this period, and the original dressings remain until the fifth day.

Wildbolz[41] described his technic of perineal prostatectomy, which differs from other perineal methods by the preservation of the external sphincter. Only a minimal part of the membranous urethra is exposed and the prostatic capsule is opened about 1 to 2 cm. below the apex of the prostate gland. Suturing between the bladder and urethra, as well as the closing of the prostatic capsule, reëstablishes the integrity of all the structures. Wildbolz did not observe continuous incontinence in 340 perineal prostatectomies, and only in 3.5 per cent was there any weakness of the bladder for a period of weeks or months. There were nine rectal fistulas, which closed spontaneously or by secondary operation. The mortality rate was 6 per cent; 74 per cent of the operative wounds healed within fourteen days and 17 per cent within three weeks.

41. Wildbolz, H.: Die Technik der perimealen Prostatektomie und ihre klinischen Erfolge. VIII. Tagung der Deutschen Gesellschaft für Urologie, Ztschr. f. urol. Chir. **26**:312, 1929.

[Compilers' Note.—Wildbolz is a strong advocate of perineal prostatectomy. His technic differs somewhat from Young's in the manner of dealing with the membranous urethra and of opening the prostatic capsule. Preservation of the external sphincter is his chief aim. Wildbolz gives as one of his main reasons for choosing the perineal route the excellent opportunity afforded for radical prostatectomy when malignancy is unexpectedly encountered in a gland which has been diagnosed as benign.]

Chute [42] stated that he prefers the two-stage suprapubic prostatectomy in the majority of cases of prostatic obstruction, but expressed the belief that the perineal route is the best for removing small fibrous prostate glands, most malignant glands, and a large proportion of hypertrophic glands in obese men.

At the time of performing the first stage, Chute usually performs double bilateral vasotomy. The second stage is performed at varying periods of from ten days to many weeks or even months later, depending mainly on the condition of the patient's kidneys and heart. Spinal anesthesia is employed for the second stage in most cases, because of its safety.

The two-stage operation has three definite advantages over the one-stage suprapubic prostatectomy, especially in case of a poor risk. It affords better opportunity for preparation of the patient as regards the kidneys; it diminishes the amount of hemorrhage encountered at the time of enucleation, and it minimizes the sepsis and sloughing of the suprapubic wound and perivesical tissues. Preliminary drainage afforded by the two-stage operation not only permits the kidneys that have been affected by back-pressure to readjust themselves to proper function, but lessens the congestion of the prostate gland and the outlet of the bladder, in this way diminishing the tendency to bleeding at the time the gland is enucleated.

Carcinoma.—Zinner [43] stated that with the characteristic rectal signs of prostatic carcinoma, a distinction must be made from prostatic calculi by roentgenograms and from prostatitis by the intramuscular injections of a nonspecific milk preparation (sterile milk in ampules). If metastasis is not present, the relation of the carcinoma to the rectal mucous membrane should be determined. If the latter is movable, a radical operation may be undertaken. Carrying out this principle by means of complete prostatectomy and resection of the trigone, he obtained good

42. Chute, A. L.: Certain Advantages of the Two-Stage Suprapubic Prostatectomy, New England J. Med. **200**:1075, 1929.

43. Zinner, A.: Beitrag zur operativen Therapie des Prostatacarcinoms. VIII. Tagung der Deutschen Gesellschaft für Urologie, Ztschr. f. urol. Chir. **26**:312, 1929.

results in 3 cases. One patient was free from recurrences for four years; then death occurred from intercurrent disease. Another patient lived two and a half years without symptoms, and a third patient lived one and a half years with local recurrence.

Cases in which the rectal mucous membrane is fixed are not amenable to radical operation. In such cases roentgen rays or radium may be tried. Results from the latter have not been satisfactory. In only a fourth of the cases is the length of life prolonged.

Hunt [44] stated that carcinoma within the substance of the prostate gland is difficult to recognize, and it may be suspected on clinical examination only when it is near the capsule and urethral surfaces of the gland. Since all prostatic tissue is not removed in the operation for benign prostatic disease, it is possible for an entirely benign adenomatous process to be removed, leaving tissue in which carcinoma may develop subsequently.

Four cases are cited by Hunt in which carcinoma developed in the prostate gland after prostatectomy. In one case carcinoma developed eighteen years after prostatectomy for benign adenomatous hypertrophy, and the time between prostatectomy and necropsy was sufficiently long to eliminate the possibility of malignant tissue having been left behind at the time of prostatectomy. Reexamination of the specimen from the first operation, which had been preserved for eighteen years, showed it to be entirely benign. In a second case evidence of malignancy appeared two years after prostatectomy. Although the final microscopic sections in this case were not available, digital examination and the roentgenographic demonstration of metastasis to the bones of the pelvis and lumbar spine indicated the presence of malignancy. In the third case evidence of malignancy appeared about six months after prostatectomy. One patient died several days after removal of the prostate gland, and at necropsy a small carcinoma was found in the prostatic capsule. In this instance definitely encapsulated, benign adenomatous hypertrophied tissue was present in association with carcinoma. The gland was readily enucleated, and on careful section failed to show any evidence of a malignant condition.

In these four cases only the first properly may be considered as a true example of a malignant growth developing subsequent to prostatectomy for benign disease. The others are probably cases in which the malignant condition was present but was not removed at the time of prostatectomy.

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44. Hunt, F. C.: Carcinoma of the Prostate Gland and Prostatic Capsule Developing Subsequent to Prostatectomy for Benign Prostatic Hypertrophy, J. Urol. **22**:351, 1929.

Bugbee [45] reported 6 cases in which small carcinomas were found in the lateral and median lobes of the prostate gland and in which the condition was diagnosed only on microscopic section after removal. A careful examination of all prostate glands may make it possible to detect small suspicious areas, indicating prostatectomy in some cases, in which otherwise palliative measures might be continued. Retention which occurs suddenly in the presence of comparatively mild urinary symptoms may suggest malignancy. Prostatectomy may be carried out as easily in these cases as in simple hypertrophy. Preliminary suprapubic drainage, allowing edema and infection to subside, is an advantage. There is evidence that the small amount of trauma incident to the removal of these prostate glands has caused a squeezing out of carcinoma cells into the lymphatics and a consequent spread of disease.

Infections.—Mitchell and Von Lackum [46] stated that it is now estimated that approximately 60 per cent of the cases of prostatitis are nongonorrheal in origin.

In male patients aged 50 years or more, with the usual degree of senile prostatic enlargement, eight or ten pus cells in each high-power microscopic field may be present but are of no clinical significance. Unsatisfactory results of radical treatment of hypertrophy of the prostate gland and associated inflammatory prostatic bar obstruction have shown that, even in advanced years, prostatic infection sometimes has a more important bearing on urinary obstruction than adenomatous enlargement of the gland. Frequently in elderly men, with nocturia as the only urinary disturbance, a few prostatic massages or the passage of a moderately sized gum elastic catheter two or three times is sufficient to give relief. This indicates that the symptoms of obstruction are of inflammatory origin, although symptomless senile enlargement may also be present. The presence of small clumps of pus cells is practically always diagnostic of prostatic infection. Several provocative treatments may be required to bring out the severity of latent prostatic infections.

In a study of cultures of the expressed prostatic secretions of 405 cases, Von Lackum found that 141 (35.25 per cent) were sterile. The size of the prostate gland and the degree of infection were not correlated; often a small, apparently insignificant gland was found to carry the highest degree of infection. In the absence of pus cells there may be organisms which are active or potentially virulent.

The diagnosis of prostatitis should not be made by digital examination alone, as it is not an infallible index of the degree of infection. In

45. Bugbee, H. G.: Cases of Unsuspected Carcinoma of the Prostate Discovered on Microscopic Section, J. Urol. **22**:363, 1929.

46. Mitchell, John, and Von Lackum, W. H.: Chronic Prostatitis and Vesiculitis: Physical and Microscopic Data, Brit. J. Urol. **1**:277, 1929.

estimating the consistence of the gland, care must be exercised not to mistake superficial edema of the structures between the examining finger and the prostate gland itself for abnormal softness of the tissue of the gland. Sometimes in prostate glands of small size there is the impression that the capsule is under tension, which is usually significant of definite prostatic infection. The globus major is thickened in most cases in which prostatitis is present. This thickening and also a distinctive tenderness may be recognized by palpation.

The seminal vesicles may be tender, enlarged, thickened and indurated, or atonicity alone may be the only palpable alteration. Along with these changes, the ampulla of the vas deferens, which normally is not palpable, may be thickened and readily palpated. The normal secretion of the seminal vesicles contains globules, and by means of them it is distinguishable macroscopically from normal prostatic secretion. The chief pathologic contents are pus cells, degenerated cells and often oily-like globules in fair number.

Stones.—Rabinovič [47] cited 2 cases of prostatic stones. In 1 case there were ninety-six stones, lying within the gland. In the second case there were three stones in the upper part of the gland; this resulted in enlargement toward the bladder giving, cystoscopically, the picture of tumor.

Rabinovič concluded that gonorrhea as an etiologic factor may be of significance. Urinary fistulas are seldom associated with prostatic calculi. In doubtful cases in which roentgenogram of the bladder shows a shadow similar to stone but not in the usual situation, differentiation must be made of a stone in a vesical diverticulum, stone in the intramural portion of the ureter, and a stone in the prostate gland. Stone in a vesical diverticulum may be recognized by means of the cystoscope and cystography. Ureteral stone may be identified by ureteral catheterization. Prostatic stone is diagnosed by excluding the foregoing conditions. The technic of the operation depends on the position of the stones.

EPIDIDYMIS, SEMINAL VESICLES AND TESTES

Tumor.—Dean [48] made a statistical study of 124 patients with teratoid tumors of the testis treated with external irradiation by means of high-voltage roentgen and radium packs.

It was noted that direct trauma preceded the formation of tumor in 11 per cent of the cases. Incomplete descent of the testis predisposes to malignant degeneration whether the testis is in the abdomen or in

47. Rabinovič, M.: Intraglanduläre Prostatasteine, Sibirsk. Arch. teor. i klin. Med. **2**:786, 1927; abstr., Ztschr. f. urol. Chir. **26**:231, 1929.

48. Dean, A. L., Jr.: The Treatment of Teratoid Tumors of the Testis with Radium and the Roentgen Ray, J. Urol. **21**:83, 1929.

the inguinal canal. With the use of Ewing's classification, the histologic diagnoses were as follows: embryonal carcinoma, 40 per cent; teratoma, 18 per cent; sarcoma, 9 per cent; cellular adenocarcinoma, 5 per cent; mixed teratoma, 2 per cent; adult cystic teratoma, 0.82 per cent; adult leiomyoma, 0.82 per cent; orchidectomy without histologic examination, 12 per cent; no operation, 11 per cent.

The first symptom in 92 per cent of the cases was a painless swelling of the testis. Other symptoms were loss of weight in 57 per cent of the cases, cramplike pain in the lower part of the abdomen in 19 per cent, pain in the back in 17 per cent, indigestion in 14 per cent, loss of strength in 14 per cent, tumor in the lower part of the abdomen in 12 per cent, constipation in 9 per cent, tenderness of testis in 8 per cent, swelling of lower limb in 5 per cent, mass in the epigastrium in 4 per cent, swelling in the left side of the neck in 4 per cent and vomiting in 2 per cent. Metastasis occurred in the abdomen of the affected side in 69 per cent of the cases, in the left supraclavicular fossa in 9 per cent, in the lungs in 8 per cent, in the epigastrium in 7 per cent, in the mediastinum in 3 per cent, in the liver in 2 per cent, in the kidney in 1 per cent, in the spleen in 0.6 per cent, in the breast of the opposite side in 0.6 per cent and in the brain in 0.6 per cent.

Dean considered it important that in the examination of intrascrotal tumors the possibility of teratoma should be kept in mind. Careful palpation of the abdomen of the same side is essential.

In the treatment of most teratoid tumors of the testis, operative procedures alone offer but little hope of cure. Because of the undifferentiated nature of their cellular structures, these tumors are especially amenable to irradiation. Conversely, the tumors most lacking in malignant qualities are the least radiosensitive.

Thirteen patients in whom the condition was considered as primarily operable were not operated on, and there was no metastasis. Ten (79 per cent) are living. One patient died about eighteen months later; two patients were not traced. Two of the patients in the group refused operation and are living and well after treatment by external irradiation.

In 3 cases local recurrence followed orchidectomy. In 1 case operation was performed, and irradiation was used in all others. All the patients are living and free from disease, 1 patient for three years and six months, 1 for four years and eight months and 1 for ten years and six months.

There were 81 patients who, after orchidectomy, had inoperable local recurrences, metastasis or both. Twenty-four (30 per cent) are known to be living; 56 (70 per cent) are dead.

Eleven patients were observed soon after orchidectomy. There was no demonstrable recurrence or metastasis. Prophylactic irradiation was given. Eight patients (72 per cent) are living.

Dean concluded that when a patient has a teratoid tumor of the testis and metastasis cannot be found, the treatment of choice consists of thorough irradiation of the testis and abdomen of the same side, followed in from four to six weeks by orchidectomy. Several courses of irradiation should follow at as short intervals as the toleration of the patient will permit. An attempt should not be made to remove growths that have metastasized from a malignant testicular tumor. Maximal irradiation by means of the radium pack and high voltage roentgen rays offers a greater chance for permanent relief.

Tuberculosis.—Ullmann [49] considered 43 cases in which treatment by roentgen ray had a beneficial effect in genital tuberculosis in males. In most cases local signs, such as swelling and infiltration, diminished within a short time. There was also improvement in the tuberculous infection of the prostate gland, seminal vesicles and scrotum. Tuberculosis of one testis was prevented from spreading to the other by roentgen irradiation of the normal organ. Occasionally abscess formed following radiotherapy. In the etiology of epididymal tuberculosis trauma appeared to be a significant factor. Beneficial results were obtained by repeated doses of roentgen rays, with long intervals between. Radiotherapy is not a substitute for operation, but it is a good adjunct, even in cases in which complete removal is not possible.

[Compilers' Note.—This report is one of the most sanguine concerning the value of roentgen treatment in genital tuberculosis. Most American writers group this form of treatment with institutional hygienic treatment, heliotherapy and ultraviolet-ray treatment. They speak of radiotherapy as causing cicatricial encapsulation of the tuberculous focus and as being accompanied by marked atrophy of the seminiferous tubules of the testis. When controlled microscopically, which has seldom been done, the tuberculous focus is found to be not healed but merely encapsulated by scar tissue. However, this in itself may have an ameliorative effect on the process and result in improvement in the patient's general health.

Operative attack, although the subject of sharp controversy as to type, is generally the method of choice among urologists. Many observers believe that the removal of the tuberculous epididymis or kidney will be attended by subsidence of activity of the tuberculous process in the prostate gland and seminal vesicles. Young, on the other hand, takes a radical stand to the contrary, believing that the prostate gland and vesicles are the primary focus and should be treated early and directly by complete eradication.

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49. Ullmann, K.: Erfahrungen über Röntgentherapie bei der männlichen Genitaltuberkulose, Monatschr. f. Harnkrankh. u. sexuelle Hyg. **1**:161, 227, 257, 289, 1928; **2**:3, 65, 103, 1928; abstr., Ztschr. f. urol. Chir. **26**:229, 1929.

Just what will be the development in the treatment of patients with genital tuberculosis by means of the roentgen rays is a matter of conjecture. As Ullmann cautiously pointed out, it is at present hardly a substitute for operation but may be a valuable adjunct. One would anticipate marked deleterious effects on the endocrine function of the testes, a disadvantage which does not necessarily accompany surgical measures.]

Infection.—Pugh [50] stated that seminal vesiculitis is a common disease. In the acute stage its symptoms are markedly similar to those of acute appendicitis and often lead to incorrect diagnosis and appendectomy. If there are symptoms of acute appendicitis, Pugh considers it important to obtain the patient's venereal or urologic history, as well as to make a rectal examination, before contemplating removal of the appendix.

URETHRA

Rupture.—Wheeler [51] reviewed 6 cases of traumatic stricture of the urethra, and observed that rupture of the urethra occurs more frequently in the bulbous portion than in the membranous urethra. Ruptures in the bulbous urethra are more prone to develop intractable stricture than are those in the membranous portion. When rupture is in front of the triangular ligament, perineal hematoma almost invariably occurs. There is intense and ineffectual desire to urinate, with severe local pain. Extravasation of the urine is prevented by a reflex spasm of the compressor urethra muscle for several hours. The amount of bleeding from the meatus after the accident is often in inverse proportion to the amount of injury to the urethra. After the partial division, hemorrhage is likely to be more profuse and continuous; when the division is complete the retraction of the part favors hemostasis, and the line of least resistance for the escape of blood is into the cellular tissues. In this way the gravest rupture is accompanied by the large hematoma. The exact site of the rupture is not always easily ascertained. If the pelvis is broken, the rupture is more likely to take place above the triangular ligament in the region of the apex of the prostate gland. In traumatic cases of rupture of the urethra, urine is ordinarily not infected at the time of injury, and the prognosis is consequently better than in extravasation of urine behind a long-standing stricture.

Early operation is important. Wheeler uses the following technic: The patient is prepared in both the suprapubic and perineal regions. The anterior urethra is washed out but no attempt is made to pass a catheter at this stage unless there is doubt about the diagnosis. Gas is the anesthesia of choice. Perineal section is done, and the bladder is opened suprapubically. At the same time, with the finger as a guide,

50. Pugh, W. S.: Seminal Vesiculitis or Appendicitis, J. Urol. **22**:313, 1929.

51. Wheeler, W. I. deC.: Traumatic Rupture of the Urethra, Proc. Roy. Soc. Med. **22**:469, 1929.

a catheter is passed in the retrograde fashion and held in position by an assistant. Clots are removed through the perineal incision, torn muscles and brushed bits of tissue are excised by sharp dissection and bleeding is controlled. A rubber catheter is passed by way of the meatus into the perineal wound and secured to the instrument which has been passed in the retrograde fashion into the bladder. The catheter is pulled into the bladder. A long thread is attached to the eye-end of the catheter and brought out through the suprapubic drainage tube. The urethra is then sutured over the catheter and perineal wound, and closed with a small superficial drain. The catheter is changed every fourth day by fastening the eye-end of a new catheter into the outer end of the one in use at the time, and then by traction on the thread, the new catheter is drawn into the urethra while the used one is withdrawn through the suprapubic incision. At the end of two weeks the retained catheter and suprapubic drain are discarded, and instruments are not passed until both the perineal and suprapubic wounds have healed completely. The patient should have monthly examinations for a year after operation to prevent the formation of a progressive stricture.

In traumatic stricture, as distinct from gonorrheal stricture, the narrowing is extrinsic as well as intrinsic; there is fibrosis of the deep tissues of the perineum surrounding the urethra besides the irregular healing of the divided ends. If the perineal wound, in the absence of an indwelling catheter, is allowed to remain open and heal by granulation, the amount of scar tissue is greatly increased. It is Wheeler's belief that by employing the retention catheter for two weeks and avoiding perineal drainage, the patient is more comfortable, the scar in the perineum is reduced to a minimum, subsequent instrumentation is simplified and convalescence is hastened.

Young [52] reported 9 cases of fracture of the pelvis complicated by rupture of the urethra which illustrate the importance of early operation and accurate repair of the urethral defect in such cases. In cases in which operation was delayed, it was necessary to carry out extensive secondary operations to cure fistulas, and to relieve patients of incontinence of urine. If operation was performed immediately, excellent results were obtained without serious complications. Young expressed the belief that careful investigation of the urinary tract should be made in all cases of fracture of the pelvis. If the posterior urethra is ruptured, the safer procedure is to carry out anastomosis immediately if the rupture is complete, as was done in one of Young's cases, to close the defect over a catheter, as was done in a second case. With perineal and suprapubic drainage, the danger of infection is avoided and excellent results are obtained.

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52. Young, H. H.: Treatment of Complete Rupture of the Posterior Urethra, Recent or Ancient, by Anastomosis, J. Urol. **21**:417, 1929.

[Compilers' Note.—The surgical principles outlined by Wheeler in dealing with traumatic rupture of the urethra are worthy of note. Passing the catheter through a suprapubic cystotomy opening simplifies the effort to recognize at once the proximal portion of the torn urethra. A second catheter passed through the meatus and on into the bladder with the aid of the instrument passed retrograde from above serves as a splint over which the torn urethral ends may be accurately sutured. Frequent change of this catheter in the manner outlined by Wheeler serves to prevent pressure necrosis, whereas suprapubic drainage favors healing with minimal infection and allows the perineal wound to be healed with the least degree of scar formation and the least opportunity for the development of fistulas. External urethrotomy alone is often a difficult procedure when the operator dissects slowly in a cicatricial, traumatized and bloody field in an effort to secure the urethral ends. Young likewise emphasized the value of suprapubic and perineal drainage in avoiding infection. The same principle is now being applied frequently in promoting the healing of repaired vesicovaginal and other fistulas of the lower portion of the urinary tract.]

Verumontanum Changes.—Begg [53] stated that pathologic changes in the verumontanum and the posterior urethra are common causes of urinary and sexual disturbances. It is suggested that the colliculus acts as a spout which, when thrust forward by the congestion and straightening of the ejaculatory ducts, directs the stream of semen along the axis of the urethra, the cavity of the bulb acting as a distributing reservoir. The tonus of the internal sphincter is aided in its function of preventing regurgitation by the congestion and erection of the ejaculatory ducts raising the prostate gland so as to occlude the supramontant urethra. The sinus pocularis is a vestigial remnant corresponding to the vagina in the female. It is not a functioning organ, but frequently acts as a trap for infection.

Granulomas due to infection are the most common pathologic conditions found in the verumontanum and may be eradicated by fulguration. The verumontanum in its relation to sexual life has been overemphasized. The organ does not contain erectile tissue and no special nerve-endings, being similar in this respect to the surrounding urethra.

ANESTHESIA

Grodinsky and Best,[54] after a series of experiments in which cadavers were injected epidurally with methylene blue (methylthionine chloride, U. S. P.), came to the following conclusions concerning sacral anesthesia:

53. Begg, R. C.: The Verumontanum in Urinary and Sexual Disorders, Brit. J. Urol. **1**:237, 1929.

54. Grodinsky, Manuel, and Best, R. R.: Sacral Anesthesia; an Experimental and Clinical Study, J. Urol. **22**:198, 1929.

An epidural injection of 20 cc. of procaine solution is sufficient to anesthetize the fifth sacral nerve completely and the fourth partially; an injection of 30 cc. will affect the fifth, fourth and third nerves completely; an injection of 40 cc. will anesthetize the fifth, fourth and third nerves completely and the second and first less completely. When it is necessary to anesthetize the first two sacral nerves completely, more than 40 cc. (50 to 75 cc.) of procaine solution are needed. The preferable method of anesthetizing the first two sacral nerves is combining a smaller caudal injection (30 to 40 cc.) with transsacral injection of the upper two sacral foramina.

In the experience of Grodinsky and Best, it was noted that 1 per cent or weaker solutions of procaine were practically as effective as the 2 per cent or stronger solutions and are to be preferred.

When excessive perineural fat and connective tissues are present it is difficult for aqueous solutions of dye or procaine to reach the bare nerves, and the use of some more penetrating anesthetic solutions is indicated.

[Compiler's Note.—A 1 per cent solution of procaine has been found by the majority of anesthetists to be the most satisfactory. The average patient usually can stand 0.6 or 0.7 Gm. of procaine in the sacral canal without having a reaction. Weaker solutions may be injected slowly, and reactions are more readily anticipated. The use of drugs, such as sodium bicarbonate, which is supposed to make the solutions more penetrating, is not satisfactory. Anesthetization of the lower three or four sacral nerves is generally sufficient for any manipulation of the neck of the bladder or for perineal or inguinal operations. Sacral anesthesia is especially satisfactory for urologic and rectal work and deserves to be much more extensively employed.]

Jeck [55] reported on more than 600 cases in which spinal anesthesia had been given since 1920 in the urologic service at Bellevue Hospital. An analysis of postoperative deaths in 536 of these cases showed the mortality to be about 4 per cent less with spinal anesthesia than with general anesthesia. In a series of more than 900 cases in which spinal anesthesia was given by Ehrlich, there were only 2 operative deaths; in neither instance could the death be attributed directly to the anesthetic.

Jeck's series of cases of spinal anesthesia included 21 cases in which nephrectomy was performed, in 14 of which it was for tuberculous kidneys. In 16 cases the anesthesia was perfect; in 2, the patients complained of slight pain; in 2, the patients complained only after the kidney had been removed, when it became necessary to administer general anesthesia in order to close the wound, and in 1 case a general anesthetic had to be given before the kidney was removed, after forty-five minutes of operating.

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55. Jeck, H. S.: Nephrectomy under Spinal Anesthesia with Particular Reference to Nephrectomy in Renal Tuberculosis, J. Urol. **21**:61, 1929.

Jeck concluded that spinal anesthesia is successful for nephrectomy. It is especially indicated in renal tuberculosis when general anesthesia is frequently contraindicated because of pulmonary involvement. Nephrectomy is rendered comparatively easy to perform, owing to the more complete relaxation with spinal than with general anesthesia. The patient's general appearance and behavior are good indications of his condition. During operation a fall in blood pressure, even when marked, is rarely a real danger signal. Procaine in the form of Pitkin's solution usually produces a more satisfactory anesthesia than procaine alone. Postoperative ileus does not frequently occur with spinal anesthesia.

[Compilers' Note.—The application of spinal anesthesia, in spite of the apprehension with which it was used when first introduced, is rapidly becoming widespread. This has been especially true during the last three years. More careful control of the technic of administration, the use of purer drugs, and, above all, the ability to avoid or to control to a great degree the alarming vasomotor collapse by means of ephedrine have probably been the chief factors in bringing spinal anesthesia into its own.]

Henline's [56] choice of anesthesia in renal operations is combined paravertebral and local anesthesia. Preliminary medication is given of three doses of ⅛ grain (0.008 Gm.) of morphine sulphate in an ampule containing 2 cc. of a 50 per cent solution of magnesium sulphate in procaine at half-hour intervals before operation. One per cent solution of procaine, without epinephrine, has given the most satisfactory results. Injection of this solution is made below the transverse process of the vertebrae from the eighth thoracic to the second lumbar inclusive, the injection being made 5 cc. above and below each, except for the two lumbar nerves, when 10 cc. is used. This is supplemented by splanchnic analgesia and infiltration along the line of incision. More perfect anesthesia should be obtained by thus blocking each nerve twice along its course, using only a safe amount of procaine. Procaine is a safe anesthetic, provided the solution is injected slowly and not directly into the blood stream or spinal canal. The destruction of procaine in the liver is rapid, not cumulative, and has no ill effects on the kidneys.

The technic of administration of a combined paravertebral and local anesthetic is more difficult for the surgeon, but the advantages to the patient are sufficient to warrant its use. The advantages to the patient are: fluids may be taken before, during and after the operation; the anesthesia persists for an average of three and a quarter hours after operation; less postoperative opiates are required, and some patients are comfortable without any narcotic; pulmonary complications are

56. Henline, R. B.: A New Method of Paravertebral Anesthesia for Kidney Operations; Report of Thirty-Three Cases, J. Urol. **21**:27, 1929.

diminished; abdominal distention is less common and severe; nausea and vomiting are rare; the mortality rate is lessened, and convalescence begins when the patient leaves the operating table. Because of the gentleness with which tissues must be handled, the operative procedures are carefully carried out. Relaxation of the tissues is complete. The kidney may be operated on regardless of any coexisting disease with less danger than under any other anesthetic. The method of anesthesia has been proved experimentally and clinically to be practical; successful anesthesia should be expected in at least 90 per cent of operations on the kidney. Pain is not experienced if the kidney is dissected gently from its bed, or if the renal pedicle is clamped and tied.

Hermann and Dózsa [57] reported the results of paravertebral anesthesia in 1,000 operations on the kidney and ureter. Transitory or permanent disadvantages which accompany inhalation, splanchnic or spinal anesthesia are not encountered in the use of paravertebral anesthesia. Low or high blood pressure, poor renal function, cardiac lesions or pulmonary involvement are not contraindications to its use.

A markedly neurotic and apprehensive patient should not be selected for paravertebral anesthesia. The evening before operation the patient is given 0.5 Gm. of veronal. Half an hour before he is taken to the operating room, he receives an injection of 0.02 Gm. of morphine sulphate. Procaine is the most desirable anesthetic, because it is the least toxic, most reliable and least expensive. In operations on the kidney and ureter, Hermann and Dózsa block from the eighth to the twelfth dorsal nerves, that is, the last five intercostal nerves and the first lumbar nerve.

[Compilers' Note.—Regional anesthesia is in part rapidly replacing inhalation narcosis for operations on the kidney and ureter. Under the stimulus of Labat, who first popularized the method in America, paravertebral anesthesia has found acceptance in a number of clinics. Hermann and Dózsa emphasized its undisputed advantages. The technic is accompanied by excellent results and may be applied with entire satisfaction by those skilled in its use. The administration of paravertebral anesthesia, however, is painstaking and time-consuming. The recent renewed interest in spinal anesthesia, which seems to be sweeping over America, and the rapid and less difficult application in average hands, will probably cause this type of regional anesthesia to supplant paravertebral injection to some degree. Paravertebral anesthesia, when properly applied, will prove satisfactory, and it is not attended by the dangers, real or imagined, which cause the more conservative operators to approach spinal anesthesia with apprehension.]

57. Hermann, H. B., and Dózsa, Eugene: Paravertebral Anaesthesia in Urology; with a Report of Its Use in a Thousand Cases of the Kidney and Ureter, Surg. Gynec. Obst. **48**:375, 1929.

URINARY INFECTION

Campbell [58] considered some of the more common types of disease of the urinary tract in infants and children in which chronic pyuria is a predominant symptom. Age is not an etiologic factor in chronic pyuria. Urinary stasis encourages urinary infection, and may be due to organic obstruction or the result of neuromuscular disease of the urinary channels, especially the bladder and ureter. Organic obstruction of the urinary tract may be congenital or acquired. In a study of 2,420 necropsies on children at Bellevue Hospital, anomalies of the urinary tract were found in more than 7 per cent and in many of these the renal injury caused by congenital urinary obstruction was extreme. When disease is secondary to obstruction, the changes which occur above the point of obstruction are identical regardless of the character of the blockage.

The disease process in cases of obstruction and infection is one of chronic suppurative nephritis and is regularly observed in the study of sections of kidneys in cases of advanced obstruction. The usual route by which bacteria reach the urinary tract is from the blood stream through the kidneys; the origin of the bacteria is as a rule a focal infection of the upper respiratory tract, tonsils, sinuses or middle ears. The incidence of acute renal infections being preceded by acute exacerbations of such focal infections is so regular that their etiologic relationship is unquestioned. True cystitis or urethrocystitis in children in the absence of renal infection is undeniable and may cause persistent pyuria.

A tight prepuce or a tight meatus may cause obstruction, with dilatation of the entire urinary tract, as well as destruction of the kidneys. Congenital malformations of the valve of the posterior urethra are significant as the cause of urinary obstruction. These mucosal folds usually extend from some portion of the verumontanum to the lateral wall of the urethra. In some cases they are unilateral and in others they have no connection with the verumontanum but form an iris diaphragm which blocks the urethra. Injury to the urinary tract with renal destruction above the point of obstruction in these cases is usually extreme. The valves may be destroyed satisfactorily by transurethral instrumentation or by suprapubic approach. Obstruction at the renal outlet is usually the result of plugging of the opening by pelvic stone, blood clot or the debris of renal necrosis. Neuromuscular disturbances of the bladder are usually accompanied by pyuria. If there is chronic spasm of the vesical outlet, urinary retention may be severe. In the latter stages when muscular paralysis has developed, a large amount of residual urine will be found in the dilated atonic, flabby bladder.

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58. Campbell, M. F.: Chronic Pyuria in Infancy and Childhood, M. J. Rec. **130**:90, 1929.

A thorough urologic examination by the same technical methods as are employed with an adult is indicated when pyuria persists longer than four weeks, in spite of intensive systematic treatment. Such an examination includes careful urinalysis, the determination of the renal function by the phenolsulphonphthalein test, the observation of the chemical changes in the blood, roentgenograms of the urinary tract to rule out stone and spina bifida, cystography, cystoscopy, ureteral catheterization and divided renal functional tests for excretion of dye and urea, and pyelography when indicated. Children withstand urologic examination remarkably well and manifest fewer and less severe post-instrumental reactions than do adults. When completely performed these examinations will demonstrate the incorrectness of the diagnosis of chronic pyelitis on the basis of persistent pyuria and also the lesions of the urinary tract which may bring about chronic pyuria. Uncomplicated chronic inflammation of the renal pelvis does not exist, and pus originating in the upper part of the urinary tract is chiefly from the renal parenchyma. In many instances involvement of the upper part of the tract is slight or absent, whereas disease of the lower part of the urinary tract is marked.

Smith,[59] in reviewing fifty cases of renal infection, observed that peridental infections and disorders of the intestinal tract often precede or accompany the onset of pyelitis, but he was unable to determine the relationship between them. The infection often persists after the probable cause has been removed. Treatment used in one case is not always as effective in an apparently similar case. Pelvic lavage proved to be the best method of treatment; it will not clear up certain cases in which there is obstruction to drainage, but it is effective in cases in which only a minor obstruction is demonstrated. Vaccine and bacteriophage were found to have no appreciable value. Improvement in the patient's general resistance is important. In all cases in which the infection persists, a complete pyelographic and functional study of the kidneys should be instituted.

INFECTION OF THE BLOOD STREAM

Scott[60] has observed that transitory infection of the blood, or bacteremia, is more common in diseases of the genito-urinary tract than true septicemia. Of 82 patients, 62 per cent had infection of the blood stream after operation. The urethra was thought to be the portal of entry in 80 per cent of the cases. Seventy-seven per cent of the patients had bacillary infection, and 23 per cent coccal infection of the blood stream. Infection by colon bacillus occurred in 40 per

59. Smith, G. G.: Fifty Cases of Renal Infection, New England J. Med. **200**:867, 1929.

60. Scott, W. W.: Blood Stream Infections in Urology; a Report of Eighty-Two Cases, J. Urol. **21**:527, 1929.

cent of the cases. Eighteen per cent of the patients died; in 74 per cent of these, infections were postoperative in origin and occurred in patients who were relatively poor operative risks.

In cases of true septicemia attempts should be made to locate and eliminate, when possible, the primary focus of infection. In the presence of preoperative or postoperative sepsis, whether or not cultures of the blood are positive, intravenous treatment may often be helpful. Scott expressed the belief that every precaution should be taken to prevent the possibility of infection of the blood stream in urologic cases.

[Compilers' Note.—Urethral fever, after cystoscopic examination and after operation with chills and fever, may serve to turn the tide against a patient who is already a poor risk. The demonstration of positive cultures of the blood in such cases does much to clear up our understanding of the mechanism of such infections, as well as to emphasize their gravity. The fact that 18 per cent of Scott's patients died postoperatively demonstrates the seriousness of the condition. If, as this article seems to bring out, bacteremia is usually transient, then it is of the utmost importance to use intensive treatment to support the patient's resistance to the highest possible level. This may be accomplished by stimulating the elimination, by supporting the cardiovascular system, by intravenous treatment, perhaps, and by establishing proper drainage of the urinary tract.]

URINARY EXTRAVASATION

Campbell [61] stated that periurethral phlegmon is a rapidly fulminating infection, with a mortality rate of approximately 50 per cent. During the last fourteen years, 135 patients with this disease have been admitted to Bellevue Hospital. Early recognition of the lesion, together with immediate institution of proper treatment, is of prime importance.

For anatomic reasons, urinary extravasation is a disease peculiar to males. Urethras scarred and ulcerated by infections past and present, weakened and dilated by long-continued urinary back-pressure secondary to stricture offered the least resistance to infectious exacerbations.

The prognosis depends on the virulence of the invading organisms, the site and duration of the disease and the degree of renal injury which has occurred. The condition should be treated by radical surgical measures, which are always emergency procedures. Free drainage should be given the urinary bladder, with wide incision and drainage of the involved tissues. Genital cutaneous repair is rapid and satisfactory. When stricture is demonstrated, periodic dilatation with sounds should

61. Campbell, M. F.: Periurethral Phlegmon (Urinary Extravasation), Surg. Gynec. Obst. **48**:382, 1929.

be used consistently after operation, as is customary for all strictures of the urethra. This treatment is the only prophylaxis against future phlegmons.

SPINA BIFIDA OCCULTA

Mertz and Smith [62] stated that it is not the bony defect itself which causes the remote nervous symptoms in spina bifida occulta, but also the nerve fibers of the cauda being adherent to the superficial structures or pressure on the cord at the point of the spinal defect. There may be a distinct meningocele protruding through the bony cleft; closure of the cleft by a tough membrane adherent to the skin; perforation of the membrane by a dense band attached to the subcutaneous tissue externally and compressing the structures of the cord internally; fatty tissue lying within the canal concealed by this membrane; bulging of the dura mater; exostosis within the canal compressing the cord structures; myofibrolipoma extending through the cleft into the bony canal, compressing the cord and its roots and degeneration of the cord tracts themselves. The presence of an added pathologic process explains why, in some case of spina bifida occulta, there are symptoms, and in another there are none. Merz and Smith consider that this fact suggests the necessity for a readjustment of the point of view concerning the significance of the presence of spina bifida occulta, and will form a basis for its consideration in the future.

The urinary symptom most frequently observed in spina bifida occulta is urinary incontinence, usually enuresis. Retention of urine in the bladder, the result of a detrusor muscle paralysis due to spina bifida occulta, with or without the loss of control of the sphincter of the bladder, has been reported.

Mertz and Smith urge the close cooperation of the urologist, the roentgenologist, and the neurologic surgeon in the detailed study of each case, as they believe that only in this way can the accurate relationship of cause and effect ultimately be determined.

PYELOGRAPHY

König [63] undertook experimental work, chiefly on dogs, to determine whether the "streak formation" often noted in pyelograms is due to the entrance of the contrast solution into the venous system of the kidney, so-called pyelovenous reflux, or whether it enters the parenchyma by way of the tubules. The phenomenon is observed in the majority

62. Mertz, H. O., and Smith, L. A.: Spina Bifida Occulta; Its Relation to Dilatations of the Upper Urinary Tract and Urinary Infections in Childhood, Radiology **12**:193, 1929.

63. König, Ernst: Ueber die sogenannten Büschelbildung im Nierenröntgenbild, Beitr. z. klin. Chir. **144**:320, 1928.

of cases at the poles of the kidney, and less frequently in the median portion, either single or multiple. This streak formation was noted in one case, that of a boy aged 17, of 128 pyelograms examined.

After the bladder had been opened by the abdominal route, the catheters were introduced into both ureters to the renal pelvis, and the bladder and abdomen were closed. To eliminate all disturbance from motion during the exposure, the animals were anesthetized and 2 cc. of a contrast medium was injected. Roentgenograms were taken, and from 2 to 6 cc. of additional fluid was then injected under rapid pressure. Roentgenograms were again taken. The animals were killed and the kidneys examined microscopically. From fifteen to thirty minutes usually elapsed between pyelography and examination of the kidneys.

As a result of these investigations, it was found that if an overfilling of the renal pelvis was produced by applying a rather high pressure, the entrance of the contrast solution into the uriniferous canals resulted, and in applying colored contrast solution under similar conditions, an experimental streak formation was observed. The streak formation consequently must be due to the entrance of the contrast medium into the uriniferous canals.

EMBOLISM

Thomas and Alyea [64] studied a group of cases in which the patients had died suddenly of pulmonary embolism after urologic operations and noted the following facts: The embolus nearly always originated in one of the femoral veins or one of its larger trunks. The thrombophlebitis of the pelvic veins, which occurred in almost every case, seldom resulted in fatal embolism. Femoral phlebitis may result from an extension of the process from the pelvic veins. The embolus arising in the femoral vein is usually dislodged before the phlebitis becomes recognizable clinically. Small emboli which cause pulmonary infarcts (usually 71 per cent) seem to come from the pelvic veins. Obese patients more than 60 years of age seem more susceptible to pulmonary embolism than others.

Mathé [65] stated that distention of the bladder or urethra with air or oxygen for any purpose may prove harmful, if not disastrous, if the air or oxygen should enter the venous circulation. Increased intravesical and intra-urethral pressure is more likely to occur in cases of prostatic hypertrophy or in cases of stricture, as it prevents the escape of air between the walls of the urethra and the indwelling catheter or cystoscope.

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64. Thomas, H. M., and Alyea, Edwin: Pulmonary Embolism Following Urological Surgery, South. M. J. **22**:737, 1929.

65. Mathé, C. P.: Fatal Embolus Due to Inflation of Bladder with Air, Surg. Gynec. Obst. **48**:429, 1929.

Mathé considers that the most effective treatment of air embolus is the immediate release of pressure of air in the bladder, artificial respiration and injection of a solution of 2 cc. of 1:1000 epinephrine directly into the right side of the heart. Death is due to the arrest of the pulmonary circulation, to gaseous distention of the right side of the heart, preventing function of the tricuspid and pulmonary valves, to too little blood reaching the left ventricle and producing anemia of the vital centers of the brain and to stasis of the coronary vessels. The use of sterile water or mild antiseptic solutions should be substituted for air in inflating the bladder and urethra for diagnostic, therapeutic and operative procedures.